

D39

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
4 October 2001 (04.10.2001)

PCT

(10) International Publication Number  
WO 01/73032 A2

(51) International Patent Classification<sup>7</sup>: C12N 15/12,  
C07K 14/47, C12N 1/21, 5/10, C07K 16/18, G01N 33/68,  
C07K 19/00, C12N 15/10, A61K 38/17, 31/70, 39/395,  
35/14, C12Q 1/68

09/709,729 9 November 2000 (09.11.2000) US

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(21) International Application Number: PCT/US01/09919

(22) International Filing Date: 27 March 2001 (27.03.2001)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

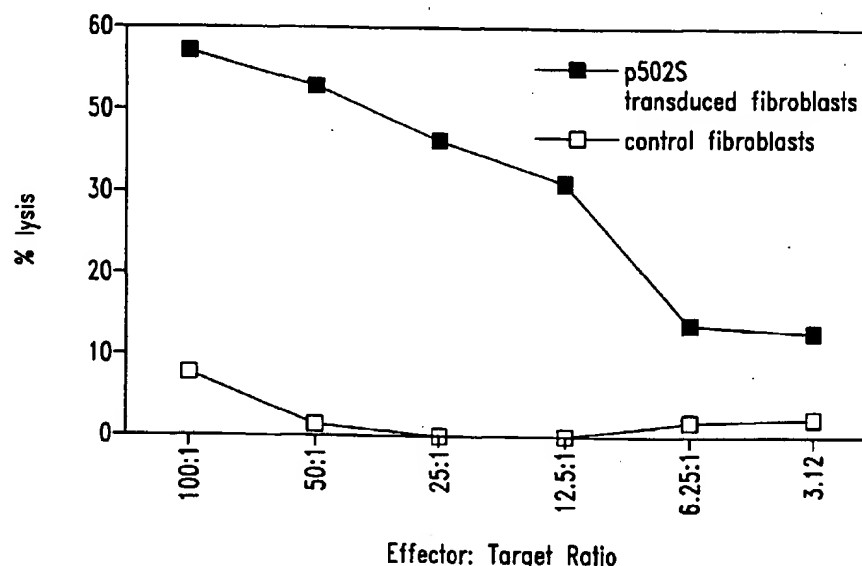
09/536,857	27 March 2000 (27.03.2000)	US
09/568,100	9 May 2000 (09.05.2000)	US
09/570,737	12 May 2000 (12.05.2000)	US
09/593,793	13 June 2000 (13.06.2000)	US
09/605,783	27 June 2000 (27.06.2000)	US
09/636,215	10 August 2000 (10.08.2000)	US
09/651,236	29 August 2000 (29.08.2000)	US
09/657,279	6 September 2000 (06.09.2000)	US
09/679,426	2 October 2000 (02.10.2000)	US
09/685,166	10 October 2000 (10.10.2000)	US

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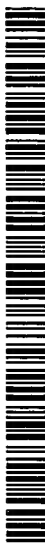
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[Continued on next page]

(54) Title: COMPOSITIONS AND METHODS FOR THE THERAPY AND DIAGNOSIS OF PROSTATE CANCER



(57) Abstract: Compositions and methods for the therapy and diagnosis of cancer, particularly prostate cancer, are disclosed. Illustrative compositions comprise one or more prostate-specific polypeptides, immunogenic portions thereof, polynucleotides that encode such polypeptides, antigen presenting cell that expresses such polypeptides, and T cells that are specific for cells expressing such polypeptides. The disclosed compositions are useful, for example, in the diagnosis, prevention and/or treatment of diseases, particularly prostate cancer.



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- (81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,

LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

- (84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

**Published:**

- without international search report and to be republished upon receipt of that report

*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*



## COMPOSITIONS AND METHODS FOR THE THERAPY AND DIAGNOSIS OF PROSTATE CANCER

### TECHNICAL FIELD OF THE INVENTION

The present invention relates generally to therapy and diagnosis of  
5 cancer, such as prostate cancer. The invention is more specifically related to  
polypeptides, comprising at least a portion of a prostate-specific protein, and to  
polynucleotides encoding such polypeptides. Such polypeptides and polynucleotides  
are useful in pharmaceutical compositions, *e.g.*, vaccines, and other compositions for  
the diagnosis and treatment of prostate cancer.

### 10 BACKGROUND OF THE INVENTION

Cancer is a significant health problem throughout the world. Although  
Cancer is a significant health problem throughout the world. Although advances have  
been made in detection and therapy of cancer, no vaccine or other universally successful  
method for prevention or treatment is currently available. Current therapies, which are  
15 generally based on a combination of chemotherapy or surgery and radiation, continue to  
prove inadequate in many patients.

Prostate cancer is the most common form of cancer among males, with  
an estimated incidence of 30% in men over the age of 50. Overwhelming clinical  
evidence shows that human prostate cancer has the propensity to metastasize to bone,  
20 and the disease appears to progress inevitably from androgen dependent to androgen  
refractory status, leading to increased patient mortality. This prevalent disease is  
currently the second leading cause of cancer death among men in the U.S.

In spite of considerable research into therapies for the disease, prostate  
cancer remains difficult to treat. Commonly, treatment is based on surgery and/or  
25 radiation therapy, but these methods are ineffective in a significant percentage of cases.  
Two previously identified prostate specific proteins - prostate specific antigen (PSA)  
and prostatic acid phosphatase (PAP) - have limited therapeutic and diagnostic  
potential. For example, PSA levels do not always correlate well with the presence of

prostate cancer, being positive in a percentage of non-prostate cancer cases, including benign prostatic hyperplasia (BPH). Furthermore, PSA measurements correlate with prostate volume, and do not indicate the level of metastasis.

In spite of considerable research into therapies for these and other  
5 cancers, prostate cancer remains difficult to diagnose and treat effectively. Accordingly, there is a need in the art for improved methods for detecting and treating such cancers. The present invention fulfills these needs and further provides other related advantages.

#### SUMMARY OF THE INVENTION

In one aspect, the present invention provides polynucleotide  
10 compositions comprising a sequence selected from the group consisting of:

(a) sequences provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and  
15 942;

(b) complements of the sequences provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-  
20 931, 938, 939 and 942;

(c) sequences consisting of at least 20 contiguous residues of a sequence provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942;  
25

(d) sequences that hybridize to a sequence provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-

606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942, under moderately stringent conditions;

(e) sequences having at least 75% identity to a sequence of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942;

(f) sequences having at least 90% identity to a sequence of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942; and

(g) degenerate variants of a sequence provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942.

In one preferred embodiment, the polynucleotide compositions of the invention are expressed in at least about 20%, more preferably in at least about 30%, and most preferably in at least about 50% of prostate tissue samples tested, at a level that is at least about 2-fold, preferably at least about 5-fold, and most preferably at least about 10-fold higher than that for other normal tissues.

The present invention, in another aspect, provides polypeptide compositions comprising an amino acid sequence that is encoded by a polynucleotide sequence described above.

The present invention further provides polypeptide compositions comprising an amino acid sequence selected from the group consisting of sequences recited in SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-551, 553-568, 573-586, 588-590, 592, 706-708, 775, 776, 778, 780, 781, 811, 814, 818, 826, 827, 853, 855,

858, 860-862, 866-877, 879, 883-893, 895, 897, 898, 909-915, 920-928, 932-934, 940, 941 and 943.

In certain preferred embodiments, the polypeptides and/or polynucleotides of the present invention are immunogenic, *i.e.*, they are capable of eliciting an immune response, particularly a humoral and/or cellular immune response, as further described herein.

The present invention further provides fragments, variants and/or derivatives of the disclosed polypeptide and/or polynucleotide sequences, wherein the fragments, variants and/or derivatives preferably have a level of immunogenic activity of at least about 50%, preferably at least about 70% and more preferably at least about 90% of the level of immunogenic activity of a polypeptide sequence set forth in SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-551, 553-568, 573-586, 588-590, 592, 706-708, 775, 776, 778, 780, 781, 811, 814, 818, 826, 827, 853, 855, 858 or 860-862, or a polypeptide sequence encoded by a polynucleotide sequence set forth in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942.

The present invention further provides polynucleotides that encode a polypeptide described above, expression vectors comprising such polynucleotides and host cells transformed or transfected with such expression vectors.

Within other aspects, the present invention provides pharmaceutical compositions comprising a polypeptide or polynucleotide as described above and a physiologically acceptable carrier.

Within a related aspect of the present invention, pharmaceutical compositions, *e.g.*, vaccine compositions, are provided for prophylactic or therapeutic applications. Such compositions generally comprise an immunogenic polypeptide or polynucleotide of the invention and an immunostimulant, such as an adjuvant, together with a physiologically acceptable carrier.

The present invention further provides pharmaceutical compositions that comprise: (a) an antibody or antigen-binding fragment thereof that specifically binds to a polypeptide of the present invention, or a fragment thereof; and (b) a physiologically acceptable carrier.

5           Within further aspects, the present invention provides pharmaceutical compositions comprising: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) a pharmaceutically acceptable carrier or excipient. Illustrative antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B cells.

10           Within related aspects, pharmaceutical compositions are provided that comprise: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) an immunostimulant.

          The present invention further provides, in other aspects, fusion proteins that comprise at least one polypeptide as described above, as well as polynucleotides  
15       encoding such fusion proteins, typically in the form of pharmaceutical compositions, *e.g.*, vaccine compositions, comprising a physiologically acceptable carrier and/or an immunostimulant. The fusions proteins may comprise multiple immunogenic polypeptides or portions/variants thereof, as described herein, and may further comprise one or more polypeptide segments for facilitating and/or enhancing the expression,  
20       purification and/or immunogenicity of the polypeptide(s).

          Within further aspects, the present invention provides methods for stimulating an immune response in a patient, preferably a T cell response in a human patient, comprising administering a pharmaceutical composition described herein. The patient may be afflicted with prostate cancer, in which case the methods provide  
25       treatment for the disease, or a patient considered to be at risk for such a disease may be treated prophylactically.

          Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient a pharmaceutical composition as recited above. The patient may be afflicted

with prostate cancer, in which case the methods provide treatment for the disease, or a patient considered to be at risk for such a disease may be treated prophylactically.

The present invention further provides, within other aspects, methods for removing tumor cells from a biological sample, comprising contacting a biological  
5 sample with T cells that specifically react with a polypeptide of the present invention, wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the polypeptide from the sample.

Within related aspects, methods are provided for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological  
10 sample treated as described above.

Methods are further provided, within other aspects, for stimulating and/or expanding T cells specific for a polypeptide of the present invention, comprising contacting T cells with one or more of: (i) a polypeptide as described above; (ii) a polynucleotide encoding such a polypeptide; and (iii) an antigen presenting cell that  
15 expresses such a polypeptide; under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells. Isolated T cell populations comprising T cells prepared as described above are also provided.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a  
20 patient an effective amount of a T cell population as described above.

The present invention further provides methods for inhibiting the development of a cancer in a patient, comprising the steps of: (a) incubating CD4<sup>+</sup> and/or CD8<sup>+</sup> T cells isolated from a patient with one or more of: (i) a polypeptide comprising at least an immunogenic portion of polypeptide disclosed herein; (ii) a  
25 polynucleotide encoding such a polypeptide; and (iii) an antigen-presenting cell that expressed such a polypeptide; and (b) administering to the patient an effective amount of the proliferated T cells, thereby inhibiting the development of a cancer in the patient. Proliferated cells may, but need not, be cloned prior to administration to the patient.

Within further aspects, the present invention provides methods for  
30 determining the presence or absence of a cancer, preferably a prostate cancer, in a

patient comprising: (a) contacting a biological sample obtained from a patient with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; and (c) comparing the amount of polypeptide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within preferred embodiments, the binding agent is an antibody, more preferably a monoclonal antibody.

The present invention also provides, within other aspects, methods for monitoring the progression of a cancer in a patient. Such methods comprise the steps of: (a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polypeptide detected in step (c) with the amount detected in step (b), and therefrom monitoring the progression of the cancer in the patient.

The present invention further provides, within other aspects, methods for determining the presence or absence of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide of the present invention; (b) detecting in the sample a level of a polynucleotide, preferably mRNA, that hybridizes to the oligonucleotide; and (c) comparing the level of polynucleotide that hybridizes to the oligonucleotide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within certain embodiments, the amount of mRNA is detected via polymerase chain reaction using, for example, at least one oligonucleotide primer that hybridizes to a polynucleotide of the present invention, or a complement of such a polynucleotide. Within other embodiments, the amount of mRNA is detected using a hybridization technique, employing an oligonucleotide probe that hybridizes to an inventive polynucleotide, or a complement of such a polynucleotide.

In related aspects, methods are provided for monitoring the progression of a cancer in a patient, comprising the steps of: (a) contacting a biological sample

obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide of the present invention; (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polynucleotide detected in step (c) with the amount detected in step (b), and therefrom monitoring the progression of the cancer in the patient.

Within further aspects, the present invention provides antibodies, such as monoclonal antibodies, that bind to a polypeptide as described above, as well as diagnostic kits comprising such antibodies. Diagnostic kits comprising one or more oligonucleotide probes or primers as described above are also provided.

These and other aspects of the present invention will become apparent upon reference to the following detailed description and attached drawings. All references disclosed herein are hereby incorporated by reference in their entirety as if each was incorporated individually.

## BRIEF DESCRIPTION OF THE DRAWINGS AND SEQUENCE IDENTIFIERS

Figure 1 illustrates the ability of T cells to kill fibroblasts expressing the representative prostate-specific polypeptide P502S, as compared to control fibroblasts. The percentage lysis is shown as a series of effector:target ratios, as indicated.

Figures 2A and 2B illustrate the ability of T cells to recognize cells expressing the representative prostate-specific polypeptide P502S. In each case, the number of  $\gamma$ -interferon spots is shown for different numbers of responders. In Figure 2A, data is presented for fibroblasts pulsed with the P2S-12 peptide, as compared to fibroblasts pulsed with a control E75 peptide. In Figure 2B, data is presented for fibroblasts expressing P502S, as compared to fibroblasts expressing HER-2/*neu*.

Figure 3 represents a peptide competition binding assay showing that the P1S#10 peptide, derived from P501S, binds HLA-A2. Peptide P1S#10 inhibits HLA-A2 restricted presentation of fluM58 peptide to CTL clone D150M58 in TNF release bioassay. D150M58 CTL is specific for the HLA-A2 binding influenza matrix peptide fluM58.



Figure 4 illustrates the ability of T cell lines generated from P1S#10 immunized mice to specifically lyse P1S#10-pulsed Jurkat A2Kb targets and P501S-transduced Jurkat A2Kb targets, as compared to EGFP-transduced Jurkat A2Kb. The percent lysis is shown as a series of effector to target ratios, as indicated.

5                Figure 5 illustrates the ability of a T cell clone to recognize and specifically lyse Jurkat A2Kb cells expressing the representative prostate-specific polypeptide P501S, thereby demonstrating that the P1S#10 peptide may be a naturally processed epitope of the P501S polypeptide.

              Figures 6A and 6B are graphs illustrating the specificity of a CD8<sup>+</sup> cell  
10    line (3A-1) for a representative prostate-specific antigen (P501S). Figure 6A shows the results of a <sup>51</sup>Cr release assay. The percent specific lysis is shown as a series of effector:target ratios, as indicated. Figure 6B shows the production of interferon-gamma by 3A-1 cells stimulated with autologous B-LCL transduced with P501S, at varying effector:target ratios as indicated.

15                Figure 7 is a Western blot showing the expression of P501S in baculovirus.

              Figure 8 illustrates the results of epitope mapping studies on P501S.

              Figure 9 is a schematic representation of the P501S protein showing the location of transmembrane domains and predicted intracellular and extracellular  
20    domains.

              Figure 10 is a genomic map showing the location of the prostate genes P775P, P704P, B305D, P712P and P774P within the Cat Eye Syndrome region of chromosome 22q11.2

              Figure 11 shows the results of an ELISA assay to determine the  
25    specificity of rabbit polyclonal antisera raised against P501S.

              Figures 12A(1), 12A(2), 12A(3), and B are the full-length cDNA (SEQ ID NO:777) and predicted amino acid (SEQ ID NO:778) sequences, respectively, for the clone P788P.

              SEQ ID NO: 1 is the determined cDNA sequence for F1-13

30                SEQ ID NO: 2 is the determined 3' cDNA sequence for F1-12

SEQ ID NO: 3 is the determined 5' cDNA sequence for F1-12  
SEQ ID NO: 4 is the determined 3' cDNA sequence for F1-16  
SEQ ID NO: 5 is the determined 3' cDNA sequence for H1-1  
SEQ ID NO: 6 is the determined 3' cDNA sequence for H1-9  
5 SEQ ID NO: 7 is the determined 3' cDNA sequence for H1-4  
SEQ ID NO: 8 is the determined 3' cDNA sequence for J1-17  
SEQ ID NO: 9 is the determined 5' cDNA sequence for J1-17  
SEQ ID NO: 10 is the determined 3' cDNA sequence for L1-12  
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SEQ ID NO: 61 is the determined cDNA sequence for P73  
30 SEQ ID NO: 62 is the determined cDNA sequence for P75

- SEQ ID NO: 63 is the determined cDNA sequence for P76  
SEQ ID NO: 64 is the determined cDNA sequence for P79  
SEQ ID NO: 65 is the determined cDNA sequence for P84  
SEQ ID NO: 66 is the determined cDNA sequence for P68  
5 SEQ ID NO: 67 is the determined cDNA sequence for P80 (also referred  
to as P704P)  
SEQ ID NO: 68 is the determined cDNA sequence for P82  
SEQ ID NO: 69 is the determined cDNA sequence for U1-3064  
SEQ ID NO: 70 is the determined cDNA sequence for U1-3065  
10 SEQ ID NO: 71 is the determined cDNA sequence for V1-3692  
SEQ ID NO: 72 is the determined cDNA sequence for 1A-3905  
SEQ ID NO: 73 is the determined cDNA sequence for V1-3686  
SEQ ID NO: 74 is the determined cDNA sequence for R1-2330  
SEQ ID NO: 75 is the determined cDNA sequence for 1B-3976  
15 SEQ ID NO: 76 is the determined cDNA sequence for V1-3679  
SEQ ID NO: 77 is the determined cDNA sequence for 1G-4736  
SEQ ID NO: 78 is the determined cDNA sequence for 1G-4738  
SEQ ID NO: 79 is the determined cDNA sequence for 1G-4741  
SEQ ID NO: 80 is the determined cDNA sequence for 1G-4744  
20 SEQ ID NO: 81 is the determined cDNA sequence for 1G-4734  
SEQ ID NO: 82 is the determined cDNA sequence for 1H-4774  
SEQ ID NO: 83 is the determined cDNA sequence for 1H-4781  
SEQ ID NO: 84 is the determined cDNA sequence for 1H-4785  
SEQ ID NO: 85 is the determined cDNA sequence for 1H-4787  
25 SEQ ID NO: 86 is the determined cDNA sequence for 1H-4796  
SEQ ID NO: 87 is the determined cDNA sequence for 1I-4807  
SEQ ID NO: 88 is the determined cDNA sequence for 1I-4810  
SEQ ID NO: 89 is the determined cDNA sequence for 1I-4811  
SEQ ID NO: 90 is the determined cDNA sequence for 1J-4876  
30 SEQ ID NO: 91 is the determined cDNA sequence for 1K-4884

- SEQ ID NO: 92 is the determined cDNA sequence for 1K-4896  
SEQ ID NO: 93 is the determined cDNA sequence for 1G-4761  
SEQ ID NO: 94 is the determined cDNA sequence for 1G-4762  
SEQ ID NO: 95 is the determined cDNA sequence for 1H-4766  
5 SEQ ID NO: 96 is the determined cDNA sequence for 1H-4770  
SEQ ID NO: 97 is the determined cDNA sequence for 1H-4771  
SEQ ID NO: 98 is the determined cDNA sequence for 1H-4772  
SEQ ID NO: 99 is the determined cDNA sequence for 1D-4297  
SEQ ID NO: 100 is the determined cDNA sequence for 1D-4309  
10 SEQ ID NO: 101 is the determined cDNA sequence for 1D.1-4278  
SEQ ID NO: 102 is the determined cDNA sequence for 1D-4288  
SEQ ID NO: 103 is the determined cDNA sequence for 1D-4283  
SEQ ID NO: 104 is the determined cDNA sequence for 1D-4304  
SEQ ID NO: 105 is the determined cDNA sequence for 1D-4296  
15 SEQ ID NO: 106 is the determined cDNA sequence for 1D-4280  
SEQ ID NO: 107 is the determined full length cDNA sequence for F1-12  
(also referred to as P504S)  
SEQ ID NO: 108 is the predicted amino acid sequence for F1-12  
SEQ ID NO: 109 is the determined full length cDNA sequence for J1-17  
20 SEQ ID NO: 110 is the determined full length cDNA sequence for L1-12  
(also referred to as P501S)  
SEQ ID NO: 111 is the determined full length cDNA sequence for N1-  
1862 (also referred to as P503S)  
SEQ ID NO: 112 is the predicted amino acid sequence for J1-17  
25 SEQ ID NO: 113 is the predicted amino acid sequence for L1-12 (also  
referred to as P501S)  
SEQ ID NO: 114 is the predicted amino acid sequence for N1-1862 (also  
referred to as P503S)  
SEQ ID NO: 115 is the determined cDNA sequence for P89  
30 SEQ ID NO: 116 is the determined cDNA sequence for P90

SEQ ID NO: 117 is the determined cDNA sequence for P92  
SEQ ID NO: 118 is the determined cDNA sequence for P95  
SEQ ID NO: 119 is the determined cDNA sequence for P98  
SEQ ID NO: 120 is the determined cDNA sequence for P102  
5 SEQ ID NO: 121 is the determined cDNA sequence for P110  
SEQ ID NO: 122 is the determined cDNA sequence for P111  
SEQ ID NO: 123 is the determined cDNA sequence for P114  
SEQ ID NO: 124 is the determined cDNA sequence for P115  
SEQ ID NO: 125 is the determined cDNA sequence for P116  
10 SEQ ID NO: 126 is the determined cDNA sequence for P124  
SEQ ID NO: 127 is the determined cDNA sequence for P126  
SEQ ID NO: 128 is the determined cDNA sequence for P130  
SEQ ID NO: 129 is the determined cDNA sequence for P133  
SEQ ID NO: 130 is the determined cDNA sequence for P138  
15 SEQ ID NO: 131 is the determined cDNA sequence for P143  
SEQ ID NO: 132 is the determined cDNA sequence for P151  
SEQ ID NO: 133 is the determined cDNA sequence for P156  
SEQ ID NO: 134 is the determined cDNA sequence for P157  
SEQ ID NO: 135 is the determined cDNA sequence for P166  
20 SEQ ID NO: 136 is the determined cDNA sequence for P176  
SEQ ID NO: 137 is the determined cDNA sequence for P178  
SEQ ID NO: 138 is the determined cDNA sequence for P179  
SEQ ID NO: 139 is the determined cDNA sequence for P185  
SEQ ID NO: 140 is the determined cDNA sequence for P192  
25 SEQ ID NO: 141 is the determined cDNA sequence for P201  
SEQ ID NO: 142 is the determined cDNA sequence for P204  
SEQ ID NO: 143 is the determined cDNA sequence for P208  
SEQ ID NO: 144 is the determined cDNA sequence for P211  
SEQ ID NO: 145 is the determined cDNA sequence for P213  
30 SEQ ID NO: 146 is the determined cDNA sequence for P219

SEQ ID NO: 147 is the determined cDNA sequence for P237  
SEQ ID NO: 148 is the determined cDNA sequence for P239  
SEQ ID NO: 149 is the determined cDNA sequence for P248  
SEQ ID NO: 150 is the determined cDNA sequence for P251  
5 SEQ ID NO: 151 is the determined cDNA sequence for P255  
SEQ ID NO: 152 is the determined cDNA sequence for P256  
SEQ ID NO: 153 is the determined cDNA sequence for P259  
SEQ ID NO: 154 is the determined cDNA sequence for P260  
SEQ ID NO: 155 is the determined cDNA sequence for P263  
10 SEQ ID NO: 156 is the determined cDNA sequence for P264  
SEQ ID NO: 157 is the determined cDNA sequence for P266  
SEQ ID NO: 158 is the determined cDNA sequence for P270  
SEQ ID NO: 159 is the determined cDNA sequence for P272  
SEQ ID NO: 160 is the determined cDNA sequence for P278  
15 SEQ ID NO: 161 is the determined cDNA sequence for P105  
SEQ ID NO: 162 is the determined cDNA sequence for P107  
SEQ ID NO: 163 is the determined cDNA sequence for P137  
SEQ ID NO: 164 is the determined cDNA sequence for P194  
SEQ ID NO: 165 is the determined cDNA sequence for P195  
20 SEQ ID NO: 166 is the determined cDNA sequence for P196  
SEQ ID NO: 167 is the determined cDNA sequence for P220  
SEQ ID NO: 168 is the determined cDNA sequence for P234  
SEQ ID NO: 169 is the determined cDNA sequence for P235  
SEQ ID NO: 170 is the determined cDNA sequence for P243  
25 SEQ ID NO: 171 is the determined cDNA sequence for P703P-DE1  
SEQ ID NO: 172 is the predicted amino acid sequence for P703P-DE1  
SEQ ID NO: 173 is the determined cDNA sequence for P703P-DE2  
SEQ ID NO: 174 is the determined cDNA sequence for P703P-DE6  
SEQ ID NO: 175 is the determined cDNA sequence for P703P-DE13  
30 SEQ ID NO: 176 is the predicted amino acid sequence for P703P-DE13

SEQ ID NO: 177 is the determined cDNA sequence for P703P-DE14

SEQ ID NO: 178 is the predicted amino acid sequence for P703P-DE14

SEQ ID NO: 179 is the determined extended cDNA sequence for 1G-

4736

5

SEQ ID NO: 180 is the determined extended cDNA sequence for 1G-

4738

SEQ ID NO: 181 is the determined extended cDNA sequence for 1G-

4741

SEQ ID NO: 182 is the determined extended cDNA sequence for 1G-

10 4744

SEQ ID NO: 183 is the determined extended cDNA sequence for 1H-

4774

SEQ ID NO: 184 is the determined extended cDNA sequence for 1H-

4781

15

SEQ ID NO: 185 is the determined extended cDNA sequence for 1H-

4785

SEQ ID NO: 186 is the determined extended cDNA sequence for 1H-

4787

SEQ ID NO: 187 is the determined extended cDNA sequence for 1H-

20 4796

SEQ ID NO: 188 is the determined extended cDNA sequence for 1I-

4807

SEQ ID NO: 189 is the determined 3' cDNA sequence for 1I-4810

SEQ ID NO: 190 is the determined 3' cDNA sequence for 1I-4811

25

SEQ ID NO: 191 is the determined extended cDNA sequence for 1J-

4876

SEQ ID NO: 192 is the determined extended cDNA sequence for 1K-

4884

SEQ ID NO: 193 is the determined extended cDNA sequence for 1K-

30 4896



- 4761 SEQ ID NO: 194 is the determined extended cDNA sequence for 1G-
- 4762 SEQ ID NO: 195 is the determined extended cDNA sequence for 1G-
- 5 4766 SEQ ID NO: 196 is the determined extended cDNA sequence for 1H-
- SEQ ID NO: 197 is the determined 3' cDNA sequence for 1H-4770
- SEQ ID NO: 198 is the determined 3' cDNA sequence for 1H-4771
- 10 4772 SEQ ID NO: 199 is the determined extended cDNA sequence for 1H-
- SEQ ID NO: 200 is the determined extended cDNA sequence for 1D-
- 4309 SEQ ID NO: 201 is the determined extended cDNA sequence for 1D.1-
- 4278 SEQ ID NO: 202 is the determined extended cDNA sequence for 1D-
- 15 4288 SEQ ID NO: 203 is the determined extended cDNA sequence for 1D-
- 4283 SEQ ID NO: 204 is the determined extended cDNA sequence for 1D-
- 20 4304 SEQ ID NO: 205 is the determined extended cDNA sequence for 1D-
- 4296 SEQ ID NO: 206 is the determined extended cDNA sequence for 1D-
- 4280 SEQ ID NO: 207 is the determined cDNA sequence for 10-d8fwd
- 25 SEQ ID NO: 208 is the determined cDNA sequence for 10-H10con
- SEQ ID NO: 209 is the determined cDNA sequence for 11-C8rev
- SEQ ID NO: 210 is the determined cDNA sequence for 7.g6fwd
- SEQ ID NO: 211 is the determined cDNA sequence for 7.g6rev
- 30 SEQ ID NO: 212 is the determined cDNA sequence for 8-b5fwd

SEQ ID NO: 213 is the determined cDNA sequence for 8-b5rev  
SEQ ID NO: 214 is the determined cDNA sequence for 8-b6fwd  
SEQ ID NO: 215 is the determined cDNA sequence for 8-b6 rev  
SEQ ID NO: 216 is the determined cDNA sequence for 8-d4fwd  
5 SEQ ID NO: 217 is the determined cDNA sequence for 8-d9rev  
SEQ ID NO: 218 is the determined cDNA sequence for 8-g3fwd  
SEQ ID NO: 219 is the determined cDNA sequence for 8-g3rev  
SEQ ID NO: 220 is the determined cDNA sequence for 8-h11 rev  
SEQ ID NO: 221 is the determined cDNA sequence for g-f12fwd  
10 SEQ ID NO: 222 is the determined cDNA sequence for g-f3rev  
SEQ ID NO: 223 is the determined cDNA sequence for P509S  
SEQ ID NO: 224 is the determined cDNA sequence for P510S  
SEQ ID NO: 225 is the determined cDNA sequence for P703DE5  
SEQ ID NO: 226 is the determined cDNA sequence for 9-A11  
15 SEQ ID NO: 227 is the determined cDNA sequence for 8-C6  
SEQ ID NO: 228 is the determined cDNA sequence for 8-H7  
SEQ ID NO: 229 is the determined cDNA sequence for JPTPN13  
SEQ ID NO: 230 is the determined cDNA sequence for JPTPN14  
SEQ ID NO: 231 is the determined cDNA sequence for JPTPN23  
20 SEQ ID NO: 232 is the determined cDNA sequence for JPTPN24  
SEQ ID NO: 233 is the determined cDNA sequence for JPTPN25  
SEQ ID NO: 234 is the determined cDNA sequence for JPTPN30  
SEQ ID NO: 235 is the determined cDNA sequence for JPTPN34  
SEQ ID NO: 236 is the determined cDNA sequence for PTPN35  
25 SEQ ID NO: 237 is the determined cDNA sequence for JPTPN36  
SEQ ID NO: 238 is the determined cDNA sequence for JPTPN38  
SEQ ID NO: 239 is the determined cDNA sequence for JPTPN39  
SEQ ID NO: 240 is the determined cDNA sequence for JPTPN40  
SEQ ID NO: 241 is the determined cDNA sequence for JPTPN41  
30 SEQ ID NO: 242 is the determined cDNA sequence for JPTPN42

SEQ ID NO: 243 is the determined cDNA sequence for JTPN45  
SEQ ID NO: 244 is the determined cDNA sequence for JTPN46  
SEQ ID NO: 245 is the determined cDNA sequence for JTPN51  
SEQ ID NO: 246 is the determined cDNA sequence for JTPN56  
5 SEQ ID NO: 247 is the determined cDNA sequence for PTPN64  
SEQ ID NO: 248 is the determined cDNA sequence for JTPN65  
SEQ ID NO: 249 is the determined cDNA sequence for JTPN67  
SEQ ID NO: 250 is the determined cDNA sequence for JTPN76  
SEQ ID NO: 251 is the determined cDNA sequence for JTPN84  
10 SEQ ID NO: 252 is the determined cDNA sequence for JTPN85  
SEQ ID NO: 253 is the determined cDNA sequence for JTPN86  
SEQ ID NO: 254 is the determined cDNA sequence for JTPN87  
SEQ ID NO: 255 is the determined cDNA sequence for JTPN88  
SEQ ID NO: 256 is the determined cDNA sequence for JP1F1  
15 SEQ ID NO: 257 is the determined cDNA sequence for JP1F2  
SEQ ID NO: 258 is the determined cDNA sequence for JP1C2  
SEQ ID NO: 259 is the determined cDNA sequence for JP1B1  
SEQ ID NO: 260 is the determined cDNA sequence for JP1B2  
SEQ ID NO: 261 is the determined cDNA sequence for JP1D3  
20 SEQ ID NO: 262 is the determined cDNA sequence for JP1A4  
SEQ ID NO: 263 is the determined cDNA sequence for JP1F5  
SEQ ID NO: 264 is the determined cDNA sequence for JP1E6  
SEQ ID NO: 265 is the determined cDNA sequence for JP1D6  
SEQ ID NO: 266 is the determined cDNA sequence for JP1B5  
25 SEQ ID NO: 267 is the determined cDNA sequence for JP1A6  
SEQ ID NO: 268 is the determined cDNA sequence for JP1E8  
SEQ ID NO: 269 is the determined cDNA sequence for JP1D7  
SEQ ID NO: 270 is the determined cDNA sequence for JP1D9  
SEQ ID NO: 271 is the determined cDNA sequence for JP1C10  
30 SEQ ID NO: 272 is the determined cDNA sequence for JP1A9

SEQ ID NO: 273 is the determined cDNA sequence for JP1F12  
SEQ ID NO: 274 is the determined cDNA sequence for JP1E12  
SEQ ID NO: 275 is the determined cDNA sequence for JP1D11  
SEQ ID NO: 276 is the determined cDNA sequence for JP1C11  
5 SEQ ID NO: 277 is the determined cDNA sequence for JP1C12  
SEQ ID NO: 278 is the determined cDNA sequence for JP1B12  
SEQ ID NO: 279 is the determined cDNA sequence for JP1A12  
SEQ ID NO: 280 is the determined cDNA sequence for JP8G2  
SEQ ID NO: 281 is the determined cDNA sequence for JP8H1  
10 SEQ ID NO: 282 is the determined cDNA sequence for JP8H2  
SEQ ID NO: 283 is the determined cDNA sequence for JP8A3  
SEQ ID NO: 284 is the determined cDNA sequence for JP8A4  
SEQ ID NO: 285 is the determined cDNA sequence for JP8C3  
SEQ ID NO: 286 is the determined cDNA sequence for JP8G4  
15 SEQ ID NO: 287 is the determined cDNA sequence for JP8B6  
SEQ ID NO: 288 is the determined cDNA sequence for JP8D6  
SEQ ID NO: 289 is the determined cDNA sequence for JP8F5  
SEQ ID NO: 290 is the determined cDNA sequence for JP8A8  
SEQ ID NO: 291 is the determined cDNA sequence for JP8C7  
20 SEQ ID NO: 292 is the determined cDNA sequence for JP8D7  
SEQ ID NO: 293 is the determined cDNA sequence for P8D8  
SEQ ID NO: 294 is the determined cDNA sequence for JP8E7  
SEQ ID NO: 295 is the determined cDNA sequence for JP8F8  
SEQ ID NO: 296 is the determined cDNA sequence for JP8G8  
25 SEQ ID NO: 297 is the determined cDNA sequence for JP8B10  
SEQ ID NO: 298 is the determined cDNA sequence for JP8C10  
SEQ ID NO: 299 is the determined cDNA sequence for JP8E9  
SEQ ID NO: 300 is the determined cDNA sequence for JP8E10  
SEQ ID NO: 301 is the determined cDNA sequence for JP8F9  
30 SEQ ID NO: 302 is the determined cDNA sequence for JP8H9

- SEQ ID NO: 303 is the determined cDNA sequence for JP8C12  
SEQ ID NO: 304 is the determined cDNA sequence for JP8E11  
SEQ ID NO: 305 is the determined cDNA sequence for JP8E12  
SEQ ID NO: 306 is the amino acid sequence for the peptide PS2#12  
5 SEQ ID NO: 307 is the determined cDNA sequence for P711P  
SEQ ID NO: 308 is the determined cDNA sequence for P712P  
SEQ ID NO: 309 is the determined cDNA sequence for CLONE23  
SEQ ID NO: 310 is the determined cDNA sequence for P774P  
SEQ ID NO: 311 is the determined cDNA sequence for P775P  
10 SEQ ID NO: 312 is the determined cDNA sequence for P715P  
SEQ ID NO: 313 is the determined cDNA sequence for P710P  
SEQ ID NO: 314 is the determined cDNA sequence for P767P  
SEQ ID NO: 315 is the determined cDNA sequence for P768P  
SEQ ID NO: 316-325 are the determined cDNA sequences of previously  
15 isolated genes  
SEQ ID NO: 326 is the determined cDNA sequence for P703PDE5  
SEQ ID NO: 327 is the predicted amino acid sequence for P703PDE5  
SEQ ID NO: 328 is the determined cDNA sequence for P703P6.26  
SEQ ID NO: 329 is the predicted amino acid sequence for P703P6.26  
20 SEQ ID NO: 330 is the determined cDNA sequence for P703PX-23  
SEQ ID NO: 331 is the predicted amino acid sequence for P703PX-23  
SEQ ID NO: 332 is the determined full length cDNA sequence for  
P509S  
SEQ ID NO: 333 is the determined extended cDNA sequence for P707P  
25 (also referred to as 11-C9)  
SEQ ID NO: 334 is the determined cDNA sequence for P714P  
SEQ ID NO: 335 is the determined cDNA sequence for P705P (also  
referred to as 9-F3)  
SEQ ID NO: 336 is the predicted amino acid sequence for P705P  
30 SEQ ID NO: 337 is the amino acid sequence of the peptide P1S#10

- SEQ ID NO: 338 is the amino acid sequence of the peptide p5  
SEQ ID NO: 339 is the predicted amino acid sequence of P509S  
SEQ ID NO: 340 is the determined cDNA sequence for P778P  
SEQ ID NO: 341 is the determined cDNA sequence for P786P  
5 SEQ ID NO: 342 is the determined cDNA sequence for P789P  
SEQ ID NO: 343 is the determined cDNA sequence for a clone showing  
homology to Homo sapiens MM46 mRNA  
SEQ ID NO: 344 is the determined cDNA sequence for a clone showing  
homology to Homo sapiens TNF-alpha stimulated ABC protein (ABC50) mRNA  
10 SEQ ID NO: 345 is the determined cDNA sequence for a clone showing  
homology to Homo sapiens mRNA for E-cadherin  
SEQ ID NO: 346 is the determined cDNA sequence for a clone showing  
homology to Human nuclear-encoded mitochondrial serine hydroxymethyltransferase  
(SHMT)  
15 SEQ ID NO: 347 is the determined cDNA sequence for a clone showing  
homology to Homo sapiens natural resistance-associated macrophage protein2  
(NRAMP2)  
SEQ ID NO: 348 is the determined cDNA sequence for a clone showing  
homology to Homo sapiens phosphoglucomutase-related protein (PGMRP)  
20 SEQ ID NO: 349 is the determined cDNA sequence for a clone showing  
homology to Human mRNA for proteosome subunit p40  
SEQ ID NO: 350 is the determined cDNA sequence for P777P  
SEQ ID NO: 351 is the determined cDNA sequence for P779P  
SEQ ID NO: 352 is the determined cDNA sequence for P790P  
25 SEQ ID NO: 353 is the determined cDNA sequence for P784P  
SEQ ID NO: 354 is the determined cDNA sequence for P776P  
SEQ ID NO: 355 is the determined cDNA sequence for P780P  
SEQ ID NO: 356 is the determined cDNA sequence for P544S  
SEQ ID NO: 357 is the determined cDNA sequence for P745S  
30 SEQ ID NO: 358 is the determined cDNA sequence for P782P

- SEQ ID NO: 359 is the determined cDNA sequence for P783P
- SEQ ID NO: 360 is the determined cDNA sequence for unknown 17984
- SEQ ID NO: 361 is the determined cDNA sequence for P787P
- SEQ ID NO: 362 is the determined cDNA sequence for P788P
- 5 SEQ ID NO: 363 is the determined cDNA sequence for unknown 17994
- SEQ ID NO: 364 is the determined cDNA sequence for P781P
- SEQ ID NO: 365 is the determined cDNA sequence for P785P
- SEQ ID NO: 366-375 are the determined cDNA sequences for splice variants of B305D.
- 10 SEQ ID NO: 376 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 366.
- SEQ ID NO: 377 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 372.
- SEQ ID NO: 378 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 373.
- 15 SEQ ID NO: 379 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 374.
- SEQ ID NO: 380 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 375.
- 20 SEQ ID NO: 381 is the determined cDNA sequence for B716P.
- SEQ ID NO: 382 is the determined full-length cDNA sequence for P711P.
- SEQ ID NO: 383 is the predicted amino acid sequence for P711P.
- SEQ ID NO: 384 is the cDNA sequence for P1000C.
- 25 SEQ ID NO: 385 is the cDNA sequence for CGI-82.
- SEQ ID NO: 386 is the cDNA sequence for 23320.
- SEQ ID NO: 387 is the cDNA sequence for CGI-69.
- SEQ ID NO: 388 is the cDNA sequence for L-idoitol-2-dehydrogenase.
- SEQ ID NO: 389 is the cDNA sequence for 23379.
- 30 SEQ ID NO: 390 is the cDNA sequence for 23381.

SEQ ID NO:391 is the cDNA sequence for KIAA0122.

SEQ ID NO:392 is the cDNA sequence for 23399.

SEQ ID NO:393 is the cDNA sequence for a previously identified gene.

SEQ ID NO:394 is the cDNA sequence for HCLBP.

5 SEQ ID NO:395 is the cDNA sequence for transglutaminase.

SEQ ID NO:396 is the cDNA sequence for a previously identified gene.

SEQ ID NO:397 is the cDNA sequence for PAP.

SEQ ID NO:398 is the cDNA sequence for Ets transcription factor

PDEF.

10 SEQ ID NO:399 is the cDNA sequence for hTGR.

SEQ ID NO:400 is the cDNA sequence for KIAA0295.

SEQ ID NO:401 is the cDNA sequence for 22545.

SEQ ID NO:402 is the cDNA sequence for 22547.

SEQ ID NO:403 is the cDNA sequence for 22548.

15 SEQ ID NO:404 is the cDNA sequence for 22550.

SEQ ID NO:405 is the cDNA sequence for 22551.

SEQ ID NO:406 is the cDNA sequence for 22552.

SEQ ID NO:407 is the cDNA sequence for 22553 (also known as

P1020C).

20 SEQ ID NO:408 is the cDNA sequence for 22558.

SEQ ID NO:409 is the cDNA sequence for 22562.

SEQ ID NO:410 is the cDNA sequence for 22565.

SEQ ID NO:411 is the cDNA sequence for 22567.

SEQ ID NO:412 is the cDNA sequence for 22568.

25 SEQ ID NO:413 is the cDNA sequence for 22570.

SEQ ID NO:414 is the cDNA sequence for 22571.

SEQ ID NO:415 is the cDNA sequence for 22572.

SEQ ID NO:416 is the cDNA sequence for 22573.

SEQ ID NO:417 is the cDNA sequence for 22573.

30 SEQ ID NO:418 is the cDNA sequence for 22575.



SEQ ID NO:419 is the cDNA sequence for 22580.  
SEQ ID NO:420 is the cDNA sequence for 22581.  
SEQ ID NO:421 is the cDNA sequence for 22582.  
SEQ ID NO:422 is the cDNA sequence for 22583.  
5 SEQ ID NO:423 is the cDNA sequence for 22584.  
SEQ ID NO:424 is the cDNA sequence for 22585.  
SEQ ID NO:425 is the cDNA sequence for 22586.  
SEQ ID NO:426 is the cDNA sequence for 22587.  
SEQ ID NO:427 is the cDNA sequence for 22588.  
10 SEQ ID NO:428 is the cDNA sequence for 22589.  
SEQ ID NO:429 is the cDNA sequence for 22590.  
SEQ ID NO:430 is the cDNA sequence for 22591.  
SEQ ID NO:431 is the cDNA sequence for 22592.  
SEQ ID NO:432 is the cDNA sequence for 22593.  
15 SEQ ID NO:433 is the cDNA sequence for 22594.  
SEQ ID NO:434 is the cDNA sequence for 22595.  
SEQ ID NO:435 is the cDNA sequence for 22596.  
SEQ ID NO:436 is the cDNA sequence for 22847.  
SEQ ID NO:437 is the cDNA sequence for 22848.  
20 SEQ ID NO:438 is the cDNA sequence for 22849.  
SEQ ID NO:439 is the cDNA sequence for 22851.  
SEQ ID NO:440 is the cDNA sequence for 22852.  
SEQ ID NO:441 is the cDNA sequence for 22853.  
SEQ ID NO:442 is the cDNA sequence for 22854.  
25 SEQ ID NO:443 is the cDNA sequence for 22855.  
SEQ ID NO:444 is the cDNA sequence for 22856.  
SEQ ID NO:445 is the cDNA sequence for 22857.  
SEQ ID NO:446 is the cDNA sequence for 23601.  
SEQ ID NO:447 is the cDNA sequence for 23602.  
30 SEQ ID NO:448 is the cDNA sequence for 23605.

- SEQ ID NO:449 is the cDNA sequence for 23606.
- SEQ ID NO:450 is the cDNA sequence for 23612.
- SEQ ID NO:451 is the cDNA sequence for 23614.
- SEQ ID NO:452 is the cDNA sequence for 23618.
- 5 SEQ ID NO:453 is the cDNA sequence for 23622.
- SEQ ID NO:454 is the cDNA sequence for folate hydrolase.
- SEQ ID NO:455 is the cDNA sequence for LIM protein.
- SEQ ID NO:456 is the cDNA sequence for a known gene.
- SEQ ID NO:457 is the cDNA sequence for a known gene.
- 10 SEQ ID NO:458 is the cDNA sequence for a previously identified gene.
- SEQ ID NO:459 is the cDNA sequence for 23045.
- SEQ ID NO:460 is the cDNA sequence for 23032.
- SEQ ID NO:461 is the cDNA sequence for clone 23054.
- SEQ ID NO:462-467 are cDNA sequences for known genes.
- 15 SEQ ID NO:468-471 are cDNA sequences for P710P.
- SEQ ID NO:472 is a cDNA sequence for P1001C.
- SEQ ID NO: 473 is the determined cDNA sequence for a first splice variant of P775P (referred to as 27505).
- SEQ ID NO: 474 is the determined cDNA sequence for a second splice variant of P775P (referred to as 19947).
- 20 SEQ ID NO: 475 is the determined cDNA sequence for a third splice variant of P775P (referred to as 19941).
- SEQ ID NO: 476 is the determined cDNA sequence for a fourth splice variant of P775P (referred to as 19937).
- 25 SEQ ID NO: 477 is a first predicted amino acid sequence encoded by the sequence of SEQ ID NO: 474.
- SEQ ID NO: 478 is a second predicted amino acid sequence encoded by the sequence of SEQ ID NO: 474.
- SEQ ID NO: 479 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 475.
- 30

SEQ ID NO: 480 is a first predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.

SEQ ID NO: 481 is a second predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.

5           SEQ ID NO: 482 is a third predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.

SEQ ID NO: 483 is a fourth predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.

10           SEQ ID NO: 484 is the first 30 amino acids of the *M. tuberculosis* antigen Ra12.

SEQ ID NO: 485 is the PCR primer AW025.

SEQ ID NO: 486 is the PCR primer AW003.

SEQ ID NO: 487 is the PCR primer AW027.

SEQ ID NO: 488 is the PCR primer AW026.

15           SEQ ID NO: 489-501 are peptides employed in epitope mapping studies.

SEQ ID NO: 502 is the determined cDNA sequence of the complementarity determining region for the anti-P503S monoclonal antibody 20D4.

SEQ ID NO: 503 is the determined cDNA sequence of the complementarity determining region for the anti-P503S monoclonal antibody JA1.

20           SEQ ID NO: 504 & 505 are peptides employed in epitope mapping studies.

SEQ ID NO: 506 is the determined cDNA sequence of the complementarity determining region for the anti-P703P monoclonal antibody 8H2.

25           SEQ ID NO: 507 is the determined cDNA sequence of the complementarity determining region for the anti-P703P monoclonal antibody 7H8.

SEQ ID NO: 508 is the determined cDNA sequence of the complementarity determining region for the anti-P703P monoclonal antibody 2D4.

SEQ ID NO: 509-522 are peptides employed in epitope mapping studies.

30           SEQ ID NO: 523 is a mature form of P703P used to raise antibodies against P703P.

SEQ ID NO: 524 is the putative full-length cDNA sequence of P703P.

SEQ ID NO: 525 is the predicted amino acid sequence encoded by SEQ ID NO: 524.

SEQ ID NO: 526 is the full-length cDNA sequence for P790P.

5 SEQ ID NO: 527 is the predicted amino acid sequence for P790P.

SEQ ID NO: 528 & 529 are PCR primers.

SEQ ID NO: 530 is the cDNA sequence of a splice variant of SEQ ID NO: 366.

10 SEQ ID NO: 531 is the cDNA sequence of the open reading frame of SEQ ID NO: 530.

SEQ ID NO: 532 is the predicted amino acid encoded by the sequence of SEQ ID NO: 531.

SEQ ID NO: 533 is the DNA sequence of a putative ORF of P775P.

15 SEQ ID NO: 534 is the predicted amino acid sequence encoded by SEQ ID NO: 533.

SEQ ID NO: 535 is a first full-length cDNA sequence for P510S.

SEQ ID NO: 536 is a second full-length cDNA sequence for P510S.

SEQ ID NO: 537 is the predicted amino acid sequence encoded by SEQ ID NO: 535.

20 SEQ ID NO: 538 is the predicted amino acid sequence encoded by SEQ ID NO: 536.

SEQ ID NO: 539 is the peptide P501S-370.

SEQ ID NO: 540 is the peptide P501S-376.

SEQ ID NO: 541-551 are epitopes of P501S.

25 SEQ ID NO: 552 is an extended cDNA sequence for P712P.

SEQ ID NO: 553-568 are the amino acid sequences encoded by predicted open reading frames within SEQ ID NO: 552.

SEQ ID NO: 569 is an extended cDNA sequence for P776P.

30 SEQ ID NO: 570 is the determined cDNA sequence for a splice variant of P776P referred to as contig 6.

SEQ ID NO: 571 is the determined cDNA sequence for a splice variant of P776P referred to as contig 7.

SEQ ID NO: 572 is the determined cDNA sequence for a splice variant of P776P referred to as contig 14.

5               SEQ ID NO: 573 is the amino acid sequence encoded by a first predicted ORF of SEQ ID NO: 570.

SEQ ID NO: 574 is the amino acid sequence encoded by a second predicted ORF of SEQ ID NO: 570.

10             SEQ ID NO: 575 is the amino acid sequence encoded by a predicted ORF of SEQ ID NO: 571.

SEQ ID NO: 576-586 are amino acid sequences encoded by predicted ORFs of SEQ ID NO: 569.

SEQ ID NO: 587 is a DNA consensus sequence of the sequences of P767P and P777P.

15             SEQ ID NO: 588-590 are amino acid sequences encoded by predicted ORFs of SEQ ID NO: 587.

SEQ ID NO: 591 is an extended cDNA sequence for P1020C.

SEQ ID NO: 592 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: P1020C.

20             SEQ ID NO: 593 is a splice variant of P775P referred to as 50748.

SEQ ID NO: 594 is a splice variant of P775P referred to as 50717. SEQ ID NO: 595 is a splice variant of P775P referred to as 45985.

SEQ ID NO: 596 is a splice variant of P775P referred to as 38769.

SEQ ID NO: 597 is a splice variant of P775P referred to as 37922.

25             SEQ ID NO: 598 is a splice variant of P510S referred to as 49274.

SEQ ID NO: 599 is a splice variant of P510S referred to as 39487.

SEQ ID NO: 600 is a splice variant of P504S referred to as 5167.16.

SEQ ID NO: 601 is a splice variant of P504S referred to as 5167.1.

SEQ ID NO: 602 is a splice variant of P504S referred to as 5163.46.

30             SEQ ID NO: 603 is a splice variant of P504S referred to as 5163.42.

SEQ ID NO: 604 is a splice variant of P504S referred to as 5163.34.

SEQ ID NO: 605 is a splice variant of P504S referred to as 5163.17.

SEQ ID NO: 606 is a splice variant of P501S referred to as 10640.

SEQ ID NO: 607-615 are the sequences of PCR primers.

5        SEQ ID NO: 616 is the determined cDNA sequence of a fusion of P703P  
and PSA.

SEQ ID NO: 617 is the amino acid sequence of the fusion of P703P and  
PSA.

10       SEQ ID NO: 618-689 are determined cDNA sequences of prostate-  
specific clones.

SEQ ID NO: 690 is the cDNA sequence of the gene DD3.

SEQ ID NO: 691-697 are determined cDNA sequences of prostate-  
specific clones.

SEQ ID NO: 698 is an extended cDNA sequence for P714P.

15       SEQ ID NO: 699-701 are the cDNA sequences for splice variants of  
P704P.

SEQ ID NO: 702 is the cDNA sequence of a spliced variant of P553S  
referred to as P553S-14.

20       SEQ ID NO: 703 is the cDNA sequence of a spliced variant of P553S  
referred to as P553S-12.

SEQ ID NO: 704 is the cDNA sequence of a spliced variant of P553S  
referred to as P553S-10.

SEQ ID NO: 705 is the cDNA sequence of a spliced variant of P553S  
referred to as P553S-6.

25       SEQ ID NO: 706 is the amino acid sequence encoded by SEQ ID NO:  
705.

SEQ ID NO: 707 is the amino acid sequence encoded by SEQ ID NO:  
702 SEQ ID NO: 708 is a second amino acid sequence encoded by SEQ ID NO: 702.

30       SEQ ID NO: 709-772 are determined cDNA sequences of prostate-  
specific clones.

SEQ ID NO: 773 is a first full-length cDNA sequence for prostate-specific transglutaminase gene (also referred to herein as P558S).

SEQ ID NO: 774 is a second full-length cDNA sequence for prostate-specific transglutaminase gene.

5           SEQ ID NO: 775 is the amino acid sequence encoded by the sequence of SEQ ID NO: 773.

SEQ ID NO: 776 is the amino acid sequence encoded by the sequence of SEQ ID NO: 774.

SEQ ID NO: 777 is the full-length cDNA sequence for P788P.

10           SEQ ID NO: 778 is the amino acid sequence encoded by SEQ ID NO: 777.

SEQ ID NO: 779 is the determined cDNA sequence for a polymorphic variant of P788P.

15           SEQ ID NO: 780 is the amino acid sequence encoded by SEQ ID NO: 779.

SEQ ID NO: 781 is the amino acid sequence of peptide 4 from P703P.

SEQ ID NO: 782 is the cDNA sequence that encodes peptide 4 from P703P.

20           SEQ ID NO: 783-798 are the cDNA sequence encoding epitopes of P703P.

SEQ ID NO: 799-814 are the amino acid sequences of epitopes of P703P.

SEQ ID NO: 815 and 816 are PCR primers.

25           SEQ ID NO: 817 is the cDNA sequence encoding an N-terminal portion of P788P expressed in *E. coli*.

SEQ ID NO: 818 is the amino acid sequence of the N-terminal portion of P788P expressed in *E. coli*.

SEQ ID NO: 819 is the amino acid sequence of the *M. tuberculosis* antigen Ra12.

30           SEQ ID NO: 820 and 821 are PCR primers.

SEQ ID NO: 822 is the cDNA sequence for the Ra12-P510S-C construct.

SEQ ID NO: 823 is the cDNA sequence for the P510S-C construct.

SEQ ID NO: 824 is the cDNA sequence for the P510S-E3 construct.

5 SEQ ID NO: 825 is the amino acid sequence for the Ra12-P510S-C construct.

SEQ ID NO: 826 is the amino acid sequence for the P510S-C construct.

SEQ ID NO: 827 is the amino acid sequence for the P510S-E3 construct.

SEQ ID NO: 828-833 are PCR primers.

10 SEQ ID NO: 834 is the cDNA sequence of the construct Ra12-P775P-ORF3.

SEQ ID NO: 835 is the amino acid sequence of the construct Ra12-P775P-ORF3.

SEQ ID NO: 836 and 837 are PCR primers.

15 SEQ ID NO: 838 is the determined amino acid sequence for a P703P His tag fusion protein.

SEQ ID NO: 839 is the determined cDNA sequence for a P703P His tag fusion protein.

SEQ ID NO: 840 and 841 are PCR primers.

20 SEQ ID NO: 842 is the determined amino acid sequence for a P705P His tag fusion protein.

SEQ ID NO: 843 is the determined cDNA sequence for a P705P His tag fusion protein.

SEQ ID NO: 844 and 845 are PCR primers.

25 SEQ ID NO: 846 is the determined amino acid sequence for a P711P His tag fusion protein.

SEQ ID NO: 847 is the determined cDNA sequence for a P711P His tag fusion protein.

30 SEQ ID NO: 848 is the amino acid sequence of the *M. tuberculosis* antigen Ra12.



SEQ ID NO: 849 and 850 are PCR primers.

SEQ ID NO: 851 is the determined cDNA sequence for the construct Ra12-P501S-E2.

5       SEQ ID NO: 852 is the determined amino acid sequence for the construct Ra12-P501S-E2.

SEQ ID NO: 853 is the amino acid sequence for an epitope of P501S.

SEQ ID NO: 854 is the DNA sequence encoding SEQ ID NO: 853.

SEQ ID NO: 855 is the amino acid sequence for an epitope of P501S.

SEQ ID NO: 856 is the DNA sequence encoding SEQ ID NO: 855.

10       SEQ ID NO: 857 is a peptide employed in epitope mapping studies.

SEQ ID NO: 858 is the amino acid sequence for an epitope of P501S.

SEQ ID NO: 859 is the DNA sequence encoding SEQ ID NO: 858.

SEQ ID NO: 860-862 are the amino acid sequences for CD4 epitopes of P501S.

15       SEQ ID NO: 863-865 are the DNA sequences encoding the sequences of SEQ ID NO: 860-862.

SEQ ID NO: 866-877 are the amino acid sequences for putative CTL epitopes of P703P.

SEQ ID NO: 878 is the full-length cDNA sequence for P789P.

20       SEQ ID NO: 879 is the amino acid sequence encoded by SEQ ID NO: 878.

SEQ ID NO: 880 is the determined full-length cDNA sequence for the splice variant of P776P referred to as contig 6.

25       SEQ ID NO: 881-882 are determined full-length cDNA sequences for the splice variant of P776P referred to as contig 7.

SEQ ID NO: 883-887 are amino acid sequences encoded by SEQ ID NO: 880.

SEQ ID NO: 888-893 are amino acid sequences encoded by the splice variant of P776P referred to as contig 7.

SEQ ID NO: 894 is the full-length cDNA sequence for human transmembrane protease serine 2.

SEQ ID NO: 895 is the amino acid sequence encoded by SEQ ID NO: 894.

5           SEQ ID NO: 896 is the cDNA sequence encoding the first 209 amino acids of human transmembrane protease serine 2.

SEQ ID NO: 897 is the first 209 amino acids of human transmembrane protease serine 2.

10           SEQ ID NO: 898 is the amino acid sequence of peptide 296-322 of P501S.

SEQ ID NO: 899-902 are PCR primers.

SEQ ID NO: 903 is the determined cDNA sequence of the Vb chain of a T cell receptor for the P501S-specific T cell clone 4E5.

15           SEQ ID NO: 904 is the determined cDNA sequence of the Va chain of a T cell receptor for the P501S-specific T cell clone 4E5.

SEQ ID NO: 905 is the amino acid sequence encoded by SEQ ID NO 903.

SEQ ID NO: 906 is the amino acid sequence encoded by SEQ ID NO 904.

20           SEQ ID NO: 907 is the full-length open reading frame for P768P including stop codon.

SEQ ID NO: 908 is the full-length open reading frame for P768P without stop codon.

25           SEQ ID NO: 909 is the amino acid sequence encoded by SEQ ID NO: 908.

SEQ ID NO: 910-915 are the amino acid sequences for predicted domains of P768P.

SEQ ID NO: 916 is the full-length cDNA sequence of P835P.

30           SEQ ID NO: 917 is the cDNA sequence of the previously identified clone FLJ13581.

SEQ ID NO: 918 is the cDNA sequence of the open reading frame for P835P with stop codon.

SEQ ID NO: 919 is the cDNA sequence of the open reading frame for P835P without stop codon.

5 SEQ ID NO: 920 is the full-length amino acid sequence for P835P.

SEQ ID NO: 921-928 are the amino acid sequences of extracellular and intracellular domains of P835P.

SEQ ID NO: 929 is the full-length cDNA sequence for P1000C.

10 SEQ ID NO: 930 is the cDNA sequence of the open reading frame for P1000C, including stop codon.

SEQ ID NO: 931 is the cDNA sequence of the open reading frame for P1000C, without stop codon.

SEQ ID NO: 932 is the full-length amino acid sequence for P1000C.

SEQ ID NO: 933 is amino acids 1-100 of SEQ ID NO: 932.

15 SEQ ID NO: 934 is amino acids 100-492 of SEQ ID NO: 932.

SEQ ID NO: 935-937 are PCR primers.

SEQ ID NO: 938 is the cDNA sequence of the expressed full-length P767P coding region.

20 SEQ ID NO: 939 is the cDNA sequence of an expressed truncated P767P coding region.

SEQ ID NO: 940 is the amino acid sequence encoded by SEQ ID NO: 939.

SEQ ID NO: 941 is the amino acid sequence encoded by SEQ ID NO: 938.

25 SEQ ID NO: 942 is the DNA sequence of a CD4 epitope of P703P.

SEQ ID NO: 943 is the amino acid sequence of a CD4 epitope of P703P.

## DETAILED DESCRIPTION OF THE INVENTION

The present invention is directed generally to compositions and their use in the therapy and diagnosis of cancer, particularly prostate cancer. As described further below, illustrative compositions of the present invention include, but are not restricted to, polypeptides, particularly immunogenic polypeptides, polynucleotides encoding such polypeptides, antibodies and other binding agents, antigen presenting cells (APCs) and immune system cells (*e.g.*, T cells).

The practice of the present invention will employ, unless indicated specifically to the contrary, conventional methods of virology, immunology, microbiology, molecular biology and recombinant DNA techniques within the skill of the art, many of which are described below for the purpose of illustration. Such techniques are explained fully in the literature. See, *e.g.*, Sambrook, et al. Molecular Cloning: A Laboratory Manual (2nd Edition, 1989); Maniatis et al. Molecular Cloning: A Laboratory Manual (1982); DNA Cloning: A Practical Approach, vol. I & II (D. Glover, ed.); Oligonucleotide Synthesis (N. Gait, ed., 1984); Nucleic Acid Hybridization (B. Hames & S. Higgins, eds., 1985); Transcription and Translation (B. Hames & S. Higgins, eds., 1984); Animal Cell Culture (R. Freshney, ed., 1986); Perbal, A Practical Guide to Molecular Cloning (1984).

All publications, patents and patent applications cited herein, whether *supra* or *infra*, are hereby incorporated by reference in their entirety.

As used in this specification and the appended claims, the singular forms "a," "an" and "the" include plural references unless the content clearly dictates otherwise.

Polypeptide Compositions

As used herein, the term "polypeptide" is used in its conventional meaning, *i.e.*, as a sequence of amino acids. The polypeptides are not limited to a specific length of the product; thus, peptides, oligopeptides, and proteins are included within the definition of polypeptide, and such terms may be used interchangeably herein unless specifically indicated otherwise. This term also does not refer to or exclude post-

expression modifications of the polypeptide, for example, glycosylations, acetylations, phosphorylations and the like, as well as other modifications known in the art, both naturally occurring and non-naturally occurring. A polypeptide may be an entire protein, or a subsequence thereof. Particular polypeptides of interest in the context of  
5 this invention are amino acid subsequences comprising epitopes, i.e., antigenic determinants substantially responsible for the immunogenic properties of a polypeptide and being capable of evoking an immune response.

Particularly illustrative polypeptides of the present invention comprise those encoded by a polynucleotide sequence set forth in any one of SEQ ID NOs: 1-111,  
10 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942, or a sequence that hybridizes under moderately stringent conditions, or, alternatively, under highly stringent conditions, to a polynucleotide  
15 sequence set forth in any one of SEQ ID NOs: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942. In specific embodiments, the polypeptides of the invention comprise amino acid sequences as set  
20 forth in any one of SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-551, 553-568, 573-586, 588-590, 592, 706-708, 775, 776, 778, 780, 781, 811, 814, 818, 826, 827, 853, 855, 858, 860-862, 866-877, 879, 883-893, 895, 897, 898, 909-915, 920-928, 932-934, 940, 941 and 943.

25 The polypeptides of the present invention are sometimes herein referred to as prostate-specific proteins or prostate-specific polypeptides, as an indication that their identification has been based at least in part upon their increased levels of expression in prostate tissue samples. Thus, a "prostate-specific polypeptide" or "prostate-specific protein," refers generally to a polypeptide sequence of the present  
30 invention, or a polynucleotide sequence encoding such a polypeptide, that is expressed

in a substantial proportion of prostate tissue samples, for example preferably greater than about 20%, more preferably greater than about 30%, and most preferably greater than about 50% or more of prostate tissue samples tested, at a level that is at least two fold, and preferably at least five fold, greater than the level of expression in other  
5 normal tissues, as determined using a representative assay provided herein. A prostate-specific polypeptide sequence of the invention, based upon its increased level of expression in tumor cells, has particular utility both as a diagnostic marker as well as a therapeutic target, as further described below.

In certain preferred embodiments, the polypeptides of the invention are  
10 immunogenic, *i.e.*, they react detectably within an immunoassay (such as an ELISA or T-cell stimulation assay) with antisera and/or T-cells from a patient with prostate cancer. Screening for immunogenic activity can be performed using techniques well known to the skilled artisan. For example, such screens can be performed using methods such as those described in Harlow and Lane, *Antibodies: A Laboratory*  
15 *Manual*, Cold Spring Harbor Laboratory, 1988. In one illustrative example, a polypeptide may be immobilized on a solid support and contacted with patient sera to allow binding of antibodies within the sera to the immobilized polypeptide. Unbound sera may then be removed and bound antibodies detected using, for example, <sup>125</sup>I-labeled Protein A.

As would be recognized by the skilled artisan, immunogenic portions of  
20 the polypeptides disclosed herein are also encompassed by the present invention. An "immunogenic portion," as used herein, is a fragment of an immunogenic polypeptide of the invention that itself is immunologically reactive (*i.e.*, specifically binds) with the B-cells and/or T-cell surface antigen receptors that recognize the polypeptide.  
25 Immunogenic portions may generally be identified using well known techniques, such as those summarized in Paul, *Fundamental Immunology*, 3rd ed., 243-247 (Raven Press, 1993) and references cited therein. Such techniques include screening polypeptides for the ability to react with antigen-specific antibodies, antisera and/or T-cell lines or clones. As used herein, antisera and antibodies are "antigen-specific" if they  
30 specifically bind to an antigen (*i.e.*, they react with the protein in an ELISA or other

immunoassay, and do not react detectably with unrelated proteins). Such antisera and antibodies may be prepared as described herein, and using well-known techniques.

In one preferred embodiment, an immunogenic portion of a polypeptide of the present invention is a portion that reacts with antisera and/or T-cells at a level that is not substantially less than the reactivity of the full-length polypeptide (*e.g.*, in an ELISA and/or T-cell reactivity assay). Preferably, the level of immunogenic activity of the immunogenic portion is at least about 50%, preferably at least about 70% and most preferably greater than about 90% of the immunogenicity for the full-length polypeptide. In some instances, preferred immunogenic portions will be identified that have a level of immunogenic activity greater than that of the corresponding full-length polypeptide, *e.g.*, having greater than about 100% or 150% or more immunogenic activity.

In certain other embodiments, illustrative immunogenic portions may include peptides in which an N-terminal leader sequence and/or transmembrane domain has been deleted. Other illustrative immunogenic portions will contain a small N- and/or C-terminal deletion (*e.g.*, 1-30 amino acids, preferably 5-15 amino acids), relative to the mature protein.

In another embodiment, a polypeptide composition of the invention may also comprise one or more polypeptides that are immunologically reactive with T cells and/or antibodies generated against a polypeptide of the invention, particularly a polypeptide having an amino acid sequence disclosed herein, or to an immunogenic fragment or variant thereof.

In another embodiment of the invention, polypeptides are provided that comprise one or more polypeptides that are capable of eliciting T cells and/or antibodies that are immunologically reactive with one or more polypeptides described herein, or one or more polypeptides encoded by contiguous nucleic acid sequences contained in the polynucleotide sequences disclosed herein, or immunogenic fragments or variants thereof, or to one or more nucleic acid sequences which hybridize to one or more of these sequences under conditions of moderate to high stringency.

The present invention, in another aspect, provides polypeptide fragments comprising at least about 5, 10, 15, 20, 25, 50, or 100 contiguous amino acids, or more, including all intermediate lengths, of a polypeptide composition set forth herein, such as those set forth in SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-  
5 380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-551, 553-568, 573-586, 588-590, 592, 706-708, 775, 776, 778, 780, 781, 811, 814, 818, 826, 827, 853, 855, 858, 860-862, 866-877, 879, 883-893, 895, 897, 898, 909-915, 920-928, 932-934, 940, 941 and 943, or those encoded by a polynucleotide sequence set forth in a sequence of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-  
10 335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942.

In another aspect, the present invention provides variants of the polypeptide compositions described herein. Polypeptide variants generally  
15 encompassed by the present invention will typically exhibit at least about 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% or more identity (determined as described below), along its length, to a polypeptide sequence set forth herein.

In one preferred embodiment, the polypeptide fragments and variants  
20 provided by the present invention are immunologically reactive with an antibody and/or T-cell that reacts with a full-length polypeptide specifically set forth herein.

In another preferred embodiment, the polypeptide fragments and variants provided by the present invention exhibit a level of immunogenic activity of at least about 50%, preferably at least about 70%, and most preferably at least about 90% or  
25 more of that exhibited by a full-length polypeptide sequence specifically set forth herein.

A polypeptide "variant," as the term is used herein, is a polypeptide that typically differs from a polypeptide specifically disclosed herein in one or more substitutions, deletions, additions and/or insertions. Such variants may be naturally  
30 occurring or may be synthetically generated, for example, by modifying one or more of



the above polypeptide sequences of the invention and evaluating their immunogenic activity as described herein using any of a number of techniques well known in the art.

For example, certain illustrative variants of the polypeptides of the invention include those in which one or more portions, such as an N-terminal leader  
5 sequence or transmembrane domain, have been removed. Other illustrative variants include variants in which a small portion (*e.g.*, 1-30 amino acids, preferably 5-15 amino acids) has been removed from the N- and/or C-terminal of the mature protein.

In many instances, a variant will contain conservative substitutions. A "conservative substitution" is one in which an amino acid is substituted for another  
10 amino acid that has similar properties, such that one skilled in the art of peptide chemistry would expect the secondary structure and hydrophobic nature of the polypeptide to be substantially unchanged. As described above, modifications may be made in the structure of the polynucleotides and polypeptides of the present invention and still obtain a functional molecule that encodes a variant or derivative polypeptide  
15 with desirable characteristics, *e.g.*, with immunogenic characteristics. When it is desired to alter the amino acid sequence of a polypeptide to create an equivalent, or even an improved, immunogenic variant or portion of a polypeptide of the invention, one skilled in the art will typically change one or more of the codons of the encoding DNA sequence according to Table 1.

For example, certain amino acids may be substituted for other amino  
20 acids in a protein structure without appreciable loss of interactive binding capacity with structures such as, for example, antigen-binding regions of antibodies or binding sites on substrate molecules. Since it is the interactive capacity and nature of a protein that defines that protein's biological functional activity, certain amino acid sequence  
25 substitutions can be made in a protein sequence, and, of course, its underlying DNA coding sequence, and nevertheless obtain a protein with like properties. It is thus contemplated that various changes may be made in the peptide sequences of the disclosed compositions, or corresponding DNA sequences which encode said peptides without appreciable loss of their biological utility or activity.

TABLE 1

Amino Acids			Codons						
Alanine	Ala	A	GCA	GCC	GCG	GCU			
Cysteine	Cys	C	UGC	UGU					
Aspartic acid	Asp	D	GAC	GAU					
Glutamic acid	Glu	E	GAA	GAG					
Phenylalanine	Phe	F	UUC	UUU					
Glycine	Gly	G	GGA	GGC	GGG	GGU			
Histidine	His	H	CAC	CAU					
Isoleucine	Ile	I	AUA	AUC	AUU				
Lysine	Lys	K	AAA	AAG					
Leucine	Leu	L	UUA	UUG	CUA	CUC	CUG	CUU	
Methionine	Met	M	AUG						
Asparagine	Asn	N	AAC	AAU					
Proline	Pro	P	CCA	CCC	CCG	CCU			
Glutamine	Gln	Q	CAA	CAG					
Arginine	Arg	R	AGA	AGG	CGA	CGC	CGG	CGU	
Serine	Ser	S	AGC	AGU	UCA	UCC	UCG	UCU	
Threonine	Thr	T	ACA	ACC	ACG	ACU			
Valine	Val	V	GUA	GUC	GUG	GUU			
Tryptophan	Trp	W	UGG						
Tyrosine	Tyr	Y	UAC	UAU					

In making such changes, the hydropathic index of amino acids may be considered. The importance of the hydropathic amino acid index in conferring interactive biologic function on a protein is generally understood in the art (Kyte and Doolittle, 1982, incorporated herein by reference). It is accepted that the relative hydropathic character of the amino acid contributes to the secondary structure of the resultant protein, which in turn defines the interaction of the protein with other molecules, for example, enzymes, substrates, receptors, DNA, antibodies, antigens, and the like. Each amino acid has been assigned a hydropathic index on the basis of its

hydrophobicity and charge characteristics (Kyte and Doolittle, 1982). These values are: isoleucine (+4.5); valine (+4.2); leucine (+3.8); phenylalanine (+2.8); cysteine/cystine (+2.5); methionine (+1.9); alanine (+1.8); glycine (−0.4); threonine (−0.7); serine (−0.8); tryptophan (−0.9); tyrosine (−1.3); proline (−1.6); histidine (−3.2); glutamate (−3.5);  
5 glutamine (−3.5); aspartate (−3.5); asparagine (−3.5); lysine (−3.9); and arginine (−4.5).

It is known in the art that certain amino acids may be substituted by other amino acids having a similar hydropathic index or score and still result in a protein with similar biological activity, *i.e.* still obtain a biological functionally equivalent protein. In making such changes, the substitution of amino acids whose hydropathic indices are  
10 within  $\pm 2$  is preferred, those within  $\pm 1$  are particularly preferred, and those within  $\pm 0.5$  are even more particularly preferred. It is also understood in the art that the substitution of like amino acids can be made effectively on the basis of hydrophilicity. U. S. Patent 4,554,101 (specifically incorporated herein by reference in its entirety), states that the greatest local average hydrophilicity of a protein, as governed by the hydrophilicity of  
15 its adjacent amino acids, correlates with a biological property of the protein.

As detailed in U. S. Patent 4,554,101, the following hydrophilicity values have been assigned to amino acid residues: arginine (+3.0); lysine (+3.0); aspartate (+3.0  $\pm$  1); glutamate (+3.0  $\pm$  1); serine (+0.3); asparagine (+0.2); glutamine (+0.2); glycine (0); threonine (−0.4); proline (−0.5  $\pm$  1); alanine (−0.5); histidine (−0.5); cysteine  
20 (−1.0); methionine (−1.3); valine (−1.5); leucine (−1.8); isoleucine (−1.8); tyrosine (−2.3); phenylalanine (−2.5); tryptophan (−3.4). It is understood that an amino acid can be substituted for another having a similar hydrophilicity value and still obtain a biologically equivalent, and in particular, an immunologically equivalent protein. In such changes, the substitution of amino acids whose hydrophilicity values are within  $\pm 2$   
25 is preferred, those within  $\pm 1$  are particularly preferred, and those within  $\pm 0.5$  are even more particularly preferred.

As outlined above, amino acid substitutions are generally therefore based on the relative similarity of the amino acid side-chain substituents, for example, their hydrophobicity, hydrophilicity, charge, size, and the like. Exemplary substitutions that  
30 take various of the foregoing characteristics into consideration are well known to those

of skill in the art and include: arginine and lysine; glutamate and aspartate; serine and threonine; glutamine and asparagine; and valine, leucine and isoleucine.

In addition, any polynucleotide may be further modified to increase stability *in vivo*. Possible modifications include, but are not limited to, the addition of  
5 flanking sequences at the 5' and/or 3' ends; the use of phosphorothioate or 2' O-methyl rather than phosphodiesterase linkages in the backbone; and/or the inclusion of nontraditional bases such as inosine, queosine and wybutosine, as well as acetyl-methyl-, thio- and other modified forms of adenine, cytidine, guanine, thymine and uridine.

10 Amino acid substitutions may further be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity and/or the amphipathic nature of the residues. For example, negatively charged amino acids include aspartic acid and glutamic acid; positively charged amino acids include lysine and arginine; and amino acids with uncharged polar head groups having similar hydrophilicity values  
15 include leucine, isoleucine and valine; glycine and alanine; asparagine and glutamine; and serine, threonine, phenylalanine and tyrosine. Other groups of amino acids that may represent conservative changes include: (1) ala, pro, gly, glu, asp, gln, asn, ser, thr; (2) cys, ser, tyr, thr; (3) val, ile, leu, met, ala, phe; (4) lys, arg, his; and (5) phe, tyr, trp, his. A variant may also, or alternatively, contain nonconservative changes. In a  
20 preferred embodiment, variant polypeptides differ from a native sequence by substitution, deletion or addition of five amino acids or fewer. Variants may also (or alternatively) be modified by, for example, the deletion or addition of amino acids that have minimal influence on the immunogenicity, secondary structure and hydrophobic nature of the polypeptide.

25 As noted above, polypeptides may comprise a signal (or leader) sequence at the N-terminal end of the protein, which co-translationally or post-translationally directs transfer of the protein. The polypeptide may also be conjugated to a linker or other sequence for ease of synthesis, purification or identification of the polypeptide (e.g., poly-His), or to enhance binding of the polypeptide to a solid support. For  
30 example, a polypeptide may be conjugated to an immunoglobulin Fc region.

When comparing polypeptide sequences, two sequences are said to be “identical” if the sequence of amino acids in the two sequences is the same when aligned for maximum correspondence, as described below. Comparisons between two sequences are typically performed by comparing the sequences over a comparison window to identify and compare local regions of sequence similarity. A “comparison window” as used herein, refers to a segment of at least about 20 contiguous positions, usually 30 to about 75, 40 to about 50, in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

Optimal alignment of sequences for comparison may be conducted using the Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. This program embodies several alignment schemes described in the following references: Dayhoff, M.O. (1978) A model of evolutionary change in proteins – Matrices for detecting distant relationships. In Dayhoff, M.O. (ed.) *Atlas of Protein Sequence and Structure*, National Biomedical Research Foundation, Washington DC Vol. 5, Suppl. 3, pp. 345-358; Hein J. (1990) Unified Approach to Alignment and Phylogenies pp. 626-645 *Methods in Enzymology* vol. 183, Academic Press, Inc., San Diego, CA; Higgins, D.G. and Sharp, P.M. (1989) *CABIOS* 5:151-153; Myers, E.W. and Muller W. (1988) *CABIOS* 4:11-17; Robinson, E.D. (1971) *Comb. Theor* 11:105; Santou, N. Nes, M. (1987) *Mol. Biol. Evol.* 4:406-425; Sneath, P.H.A. and Sokal, R.R. (1973) *Numerical Taxonomy – the Principles and Practice of Numerical Taxonomy*, Freeman Press, San Francisco, CA; Wilbur, W.J. and Lipman, D.J. (1983) *Proc. Natl. Acad. Sci. USA* 80:726-730.

Alternatively, optimal alignment of sequences for comparison may be conducted by the local identity algorithm of Smith and Waterman (1981) *Add. APL. Math* 2:482, by the identity alignment algorithm of Needleman and Wunsch (1970) *J. Mol. Biol.* 48:443, by the search for similarity methods of Pearson and Lipman (1988) *Proc. Natl. Acad. Sci. USA* 85: 2444, by computerized implementations of these algorithms (GAP, BESTFIT, BLAST, FASTA, and TFASTA in the Wisconsin Genetics

Software Package, Genetics Computer Group (GCG), 575 Science Dr., Madison, WI), or by inspection.

One preferred example of algorithms that are suitable for determining percent sequence identity and sequence similarity are the BLAST and BLAST 2.0 algorithms, which are described in Altschul et al. (1977) *Nucl. Acids Res.* 25:3389-3402 and Altschul et al. (1990) *J. Mol. Biol.* 215:403-410, respectively. BLAST and BLAST 2.0 can be used, for example with the parameters described herein, to determine percent sequence identity for the polynucleotides and polypeptides of the invention. Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information. For amino acid sequences, a scoring matrix can be used to calculate the cumulative score. Extension of the word hits in each direction are halted when: the cumulative alignment score falls off by the quantity X from its maximum achieved value; the cumulative score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments; or the end of either sequence is reached. The BLAST algorithm parameters W, T and X determine the sensitivity and speed of the alignment.

In one preferred approach, the "percentage of sequence identity" is determined by comparing two optimally aligned sequences over a window of comparison of at least 20 positions, wherein the portion of the polypeptide sequence in the comparison window may comprise additions or deletions (*i.e.*, gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference sequences (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical amino acid residue occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (*i.e.*, the window size) and multiplying the results by 100 to yield the percentage of sequence identity.

Within other illustrative embodiments, a polypeptide may be a fusion polypeptide that comprises multiple polypeptides as described herein, or that comprises at least one polypeptide as described herein and an unrelated sequence, such as a known

tumor protein. A fusion partner may, for example, assist in providing T helper epitopes (an immunological fusion partner), preferably T helper epitopes recognized by humans, or may assist in expressing the protein (an expression enhancer) at higher yields than the native recombinant protein. Certain preferred fusion partners are both immunological and expression enhancing fusion partners. Other fusion partners may be selected so as to increase the solubility of the polypeptide or to enable the polypeptide to be targeted to desired intracellular compartments. Still further fusion partners include affinity tags, which facilitate purification of the polypeptide.

Fusion polypeptides may generally be prepared using standard techniques, including chemical conjugation. Preferably, a fusion polypeptide is expressed as a recombinant polypeptide, allowing the production of increased levels, relative to a non-fused polypeptide, in an expression system. Briefly, DNA sequences encoding the polypeptide components may be assembled separately, and ligated into an appropriate expression vector. The 3' end of the DNA sequence encoding one polypeptide component is ligated, with or without a peptide linker, to the 5' end of a DNA sequence encoding the second polypeptide component so that the reading frames of the sequences are in phase. This permits translation into a single fusion polypeptide that retains the biological activity of both component polypeptides.

A peptide linker sequence may be employed to separate the first and second polypeptide components by a distance sufficient to ensure that each polypeptide folds into its secondary and tertiary structures. Such a peptide linker sequence is incorporated into the fusion polypeptide using standard techniques well known in the art. Suitable peptide linker sequences may be chosen based on the following factors: (1) their ability to adopt a flexible extended conformation; (2) their inability to adopt a secondary structure that could interact with functional epitopes on the first and second polypeptides; and (3) the lack of hydrophobic or charged residues that might react with the polypeptide functional epitopes. Preferred peptide linker sequences contain Gly, Asn and Ser residues. Other near neutral amino acids, such as Thr and Ala may also be used in the linker sequence. Amino acid sequences which may be usefully employed as linkers include those disclosed in Maratea et al., *Gene* 40:39-46, 1985; Murphy et al.,

*Proc. Natl. Acad. Sci. USA* 83:8258-8262, 1986; U.S. Patent No. 4,935,233 and U.S. Patent No. 4,751,180. The linker sequence may generally be from 1 to about 50 amino acids in length. Linker sequences are not required when the first and second polypeptides have non-essential N-terminal amino acid regions that can be used to  
5 separate the functional domains and prevent steric interference.

The ligated DNA sequences are operably linked to suitable transcriptional or translational regulatory elements. The regulatory elements responsible for expression of DNA are located only 5' to the DNA sequence encoding the first polypeptides. Similarly, stop codons required to end translation and  
10 transcription termination signals are only present 3' to the DNA sequence encoding the second polypeptide.

The fusion polypeptide can comprise a polypeptide as described herein together with an unrelated immunogenic protein, such as an immunogenic protein capable of eliciting a recall response. Examples of such proteins include tetanus,  
15 tuberculosis and hepatitis proteins (*see, for example, Stoute et al. New Engl. J. Med.*, 336:86-91, 1997).

In one preferred embodiment, the immunological fusion partner is derived from a *Mycobacterium* sp., such as a *Mycobacterium tuberculosis*-derived Ra12 fragment. Ra12 compositions and methods for their use in enhancing the expression  
20 and/or immunogenicity of heterologous polynucleotide/polypeptide sequences is described in U.S. Patent Application 60/158,585, the disclosure of which is incorporated herein by reference in its entirety. Briefly, Ra12 refers to a polynucleotide region that is a subsequence of a *Mycobacterium tuberculosis* MTB32A nucleic acid. MTB32A is a serine protease of 32 KD molecular weight encoded by a gene in virulent  
25 and avirulent strains of *M. tuberculosis*. The nucleotide sequence and amino acid sequence of MTB32A have been described (for example, U.S. Patent Application 60/158,585; *see also, Skeiky et al., Infection and Immun.* (1999) 67:3998-4007, incorporated herein by reference). C-terminal fragments of the MTB32A coding sequence express at high levels and remain as a soluble polypeptides throughout the  
30 purification process. Moreover, Ra12 may enhance the immunogenicity of heterologous



immunogenic polypeptides with which it is fused. One preferred Ra12 fusion polypeptide comprises a 14 KD C-terminal fragment corresponding to amino acid residues 192 to 323 of MTB32A. Other preferred Ra12 polynucleotides generally comprise at least about 15 consecutive nucleotides, at least about 30 nucleotides, at least  
5 about 60 nucleotides, at least about 100 nucleotides, at least about 200 nucleotides, or at least about 300 nucleotides that encode a portion of a Ra12 polypeptide. Ra12 polynucleotides may comprise a native sequence (*i.e.*, an endogenous sequence that encodes a Ra12 polypeptide or a portion thereof) or may comprise a variant of such a sequence. Ra12 polynucleotide variants may contain one or more substitutions,  
10 additions, deletions and/or insertions such that the biological activity of the encoded fusion polypeptide is not substantially diminished, relative to a fusion polypeptide comprising a native Ra12 polypeptide. Variants preferably exhibit at least about 70% identity, more preferably at least about 80% identity and most preferably at least about 90% identity to a polynucleotide sequence that encodes a native Ra12 polypeptide or a  
15 portion thereof.

Within other preferred embodiments, an immunological fusion partner is derived from protein D, a surface protein of the gram-negative bacterium *Haemophilus influenza B* (WO 91/18926). Preferably, a protein D derivative comprises approximately the first third of the protein (*e.g.*, the first N-terminal 100-110 amino  
20 acids), and a protein D derivative may be lipidated. Within certain preferred embodiments, the first 109 residues of a Lipoprotein D fusion partner is included on the N-terminus to provide the polypeptide with additional exogenous T-cell epitopes and to increase the expression level in *E. coli* (thus functioning as an expression enhancer). The lipid tail ensures optimal presentation of the antigen to antigen presenting cells.  
25 Other fusion partners include the non-structural protein from influenzae virus, NS1 (hemagglutinin). Typically, the N-terminal 81 amino acids are used, although different fragments that include T-helper epitopes may be used.

In another embodiment, the immunological fusion partner is the protein known as LYTA, or a portion thereof (preferably a C-terminal portion). LYTA is  
30 derived from *Streptococcus pneumoniae*, which synthesizes an N-acetyl-L-alanine

amidase known as amidase LYTA (encoded by the *LytA* gene; *Gene* 43:265-292, 1986). LYTA is an autolysin that specifically degrades certain bonds in the peptidoglycan backbone. The C-terminal domain of the LYTA protein is responsible for the affinity to the choline or to some choline analogues such as DEAE. This property has been  
5 exploited for the development of *E. coli* C-LYTA expressing plasmids useful for expression of fusion proteins. Purification of hybrid proteins containing the C-LYTA fragment at the amino terminus has been described (*see Biotechnology* 10:795-798, 1992). Within a preferred embodiment, a repeat portion of LYTA may be incorporated into a fusion polypeptide. A repeat portion is found in the C-terminal region starting at  
10 residue 178. A particularly preferred repeat portion incorporates residues 188-305.

Yet another illustrative embodiment involves fusion polypeptides, and the polynucleotides encoding them, wherein the fusion partner comprises a targeting signal capable of directing a polypeptide to the endosomal/lysosomal compartment, as described in U.S. Patent No. 5,633,234. An immunogenic polypeptide of the invention,  
15 when fused with this targeting signal, will associate more efficiently with MHC class II molecules and thereby provide enhanced in vivo stimulation of CD4<sup>+</sup> T-cells specific for the polypeptide.

Polypeptides of the invention are prepared using any of a variety of well known synthetic and/or recombinant techniques, the latter of which are further  
20 described below. Polypeptides, portions and other variants generally less than about 150 amino acids can be generated by synthetic means, using techniques well known to those of ordinary skill in the art. In one illustrative example, such polypeptides are synthesized using any of the commercially available solid-phase techniques, such as the Merrifield solid-phase synthesis method, where amino acids are sequentially added to a  
25 growing amino acid chain. *See Merrifield, J. Am. Chem. Soc.* 85:2149-2146, 1963. Equipment for automated synthesis of polypeptides is commercially available from suppliers such as Perkin Elmer/Applied BioSystems Division (Foster City, CA), and may be operated according to the manufacturer's instructions.

In general, polypeptide compositions (including fusion polypeptides) of  
30 the invention are isolated. An "isolated" polypeptide is one that is removed from its

original environment. For example, a naturally-occurring protein or polypeptide is isolated if it is separated from some or all of the coexisting materials in the natural system. Preferably, such polypeptides are also purified, *e.g.*, are at least about 90% pure, more preferably at least about 95% pure and most preferably at least about 99% pure.

#### Polynucleotide Compositions

The present invention, in other aspects, provides polynucleotide compositions. The terms "DNA" and "polynucleotide" are used essentially interchangeably herein to refer to a DNA molecule that has been isolated free of total genomic DNA of a particular species. "Isolated," as used herein, means that a polynucleotide is substantially away from other coding sequences, and that the DNA molecule does not contain large portions of unrelated coding DNA, such as large chromosomal fragments or other functional genes or polypeptide coding regions. Of course, this refers to the DNA molecule as originally isolated, and does not exclude genes or coding regions later added to the segment by the hand of man.

As will be understood by those skilled in the art, the polynucleotide compositions of this invention can include genomic sequences, extra-genomic and plasmid-encoded sequences and smaller engineered gene segments that express, or may be adapted to express, proteins, polypeptides, peptides and the like. Such segments may be naturally isolated, or modified synthetically by the hand of man.

As will be also recognized by the skilled artisan, polynucleotides of the invention may be single-stranded (coding or antisense) or double-stranded, and may be DNA (genomic, cDNA or synthetic) or RNA molecules. RNA molecules may include HnRNA molecules, which contain introns and correspond to a DNA molecule in a one-to-one manner, and mRNA molecules, which do not contain introns. Additional coding or non-coding sequences may, but need not, be present within a polynucleotide of the present invention, and a polynucleotide may, but need not, be linked to other molecules and/or support materials.

Polynucleotides may comprise a native sequence (*i.e.*, an endogenous sequence that encodes a polypeptide/protein of the invention or a portion thereof) or may comprise a sequence that encodes a variant or derivative, preferably an immunogenic variant or derivative, of such a sequence.

5 Therefore, according to another aspect of the present invention, polynucleotide compositions are provided that comprise some or all of a polynucleotide sequence set forth in any one of SEQ ID NOs: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823,  
10 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942, complements of a polynucleotide sequence set forth in any one of SEQ ID NOs: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-  
15 931, 938, 939 and 942, and degenerate variants of a polynucleotide sequence set forth in any one of SEQ ID NOs: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942. In certain preferred  
20 embodiments, the polynucleotide sequences set forth herein encode immunogenic polypeptides, as described above.

In other related embodiments, the present invention provides polynucleotide variants having substantial identity to the sequences disclosed herein in SEQ ID NOs: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-  
25 335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942, for example those comprising at least 70% sequence identity, preferably at least 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% or higher, sequence identity compared to a polynucleotide sequence of this  
30 invention using the methods described herein, (*e.g.*, BLAST analysis using standard

parameters, as described below). One skilled in this art will recognize that these values can be appropriately adjusted to determine corresponding identity of proteins encoded by two nucleotide sequences by taking into account codon degeneracy, amino acid similarity, reading frame positioning and the like.

5           Typically, polynucleotide variants will contain one or more substitutions, additions, deletions and/or insertions, preferably such that the immunogenicity of the polypeptide encoded by the variant polynucleotide is not substantially diminished relative to a polypeptide encoded by a polynucleotide sequence specifically set forth herein). The term "variants" should also be understood to encompass homologous  
10 genes of xenogenic origin.

          In additional embodiments, the present invention provides polynucleotide fragments comprising various lengths of contiguous stretches of sequence identical to, or complementary to, one or more of the sequences disclosed herein. For example, polynucleotides are provided by this invention that comprise at  
15 least about 10, 15, 20, 30, 40, 50, 75, 100, 150, 200, 300, 400, 500 or 1000 or more contiguous nucleotides of one or more of the sequences disclosed herein as well as all intermediate lengths there between. It will be readily understood that "intermediate lengths", in this context, means any length between the quoted values, such as 16, 17, 18, 19, *etc.*; 21, 22, 23, *etc.*; 30, 31, 32, *etc.*; 50, 51, 52, 53, *etc.*; 100, 101, 102, 103, *etc.*; 150, 151, 152, 153, *etc.*; including all integers through 200-500; 500-1,000, and the like.  
20

          In another embodiment of the invention, polynucleotide compositions are provided that are capable of hybridizing under moderate to high stringency conditions to a polynucleotide sequence provided herein, or a fragment thereof, or a complementary  
25 sequence thereof. Hybridization techniques are well known in the art of molecular biology. For purposes of illustration, suitable moderately stringent conditions for testing the hybridization of a polynucleotide of this invention with other polynucleotides include prewashing in a solution of 5 X SSC, 0.5% SDS, 1.0 mM EDTA (pH 8.0); hybridizing at 50°C-60°C, 5 X SSC, overnight; followed by washing twice at 65°C for  
30 20 minutes with each of 2X, 0.5X and 0.2X SSC containing 0.1% SDS. One skilled in

the art will understand that the stringency of hybridization can be readily manipulated, such as by altering the salt content of the hybridization solution and/or the temperature at which the hybridization is performed. For example, in another embodiment, suitable highly stringent hybridization conditions include those described above, with the  
5 exception that the temperature of hybridization is increased, *e.g.*, to 60-65°C or 65-70°C.

In certain preferred embodiments, the polynucleotides described above, *e.g.*, polynucleotide variants, fragments and hybridizing sequences, encode polypeptides that are immunologically cross-reactive with a polypeptide sequence specifically set  
10 forth herein. In other preferred embodiments, such polynucleotides encode polypeptides that have a level of immunogenic activity of at least about 50%, preferably at least about 70%, and more preferably at least about 90% of that for a polypeptide sequence specifically set forth herein.

The polynucleotides of the present invention, or fragments thereof,  
15 regardless of the length of the coding sequence itself, may be combined with other DNA sequences, such as promoters, polyadenylation signals, additional restriction enzyme sites, multiple cloning sites, other coding segments, and the like, such that their overall length may vary considerably. It is therefore contemplated that a nucleic acid fragment of almost any length may be employed, with the total length preferably being limited by  
20 the ease of preparation and use in the intended recombinant DNA protocol. For example, illustrative polynucleotide segments with total lengths of about 10,000, about 5000, about 3000, about 2,000, about 1,000, about 500, about 200, about 100, about 50 base pairs in length, and the like, (including all intermediate lengths) are contemplated to be useful in many implementations of this invention.

25 When comparing polynucleotide sequences, two sequences are said to be "identical" if the sequence of nucleotides in the two sequences is the same when aligned for maximum correspondence, as described below. Comparisons between two sequences are typically performed by comparing the sequences over a comparison window to identify and compare local regions of sequence similarity. A "comparison  
30 window" as used herein, refers to a segment of at least about 20 contiguous positions,

usually 30 to about 75, preferably 40 to about 50, in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

Optimal alignment of sequences for comparison may be conducted using the Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. This program embodies several alignment schemes described in the following references: Dayhoff, M.O. (1978) A model of evolutionary change in proteins – Matrices for detecting distant relationships. In Dayhoff, M.O. (ed.) *Atlas of Protein Sequence and Structure*, National Biomedical Research Foundation, Washington DC Vol. 5, Suppl. 3, pp. 345-358; Hein J. (1990) Unified Approach to Alignment and Phylogenies pp. 626-645 *Methods in Enzymology* vol. 183, Academic Press, Inc., San Diego, CA; Higgins, D.G. and Sharp, P.M. (1989) *CABIOS* 5:151-153; Myers, E.W. and Muller W. (1988) *CABIOS* 4:11-17; Robinson, E.D. (1971) *Comb. Theor* 11:105; Santou, N. Nes, M. (1987) *Mol. Biol. Evol.* 4:406-425; Sneath, P.H.A. and Sokal, R.R. (1973) *Numerical Taxonomy – the Principles and Practice of Numerical Taxonomy*, Freeman Press, San Francisco, CA; Wilbur, W.J. and Lipman, D.J. (1983) *Proc. Natl. Acad., Sci. USA* 80:726-730.

Alternatively, optimal alignment of sequences for comparison may be conducted by the local identity algorithm of Smith and Waterman (1981) *Add. APL. Math* 2:482, by the identity alignment algorithm of Needleman and Wunsch (1970) *J. Mol. Biol.* 48:443, by the search for similarity methods of Pearson and Lipman (1988) *Proc. Natl. Acad. Sci. USA* 85: 2444, by computerized implementations of these algorithms (GAP, BESTFIT, BLAST, FASTA, and TFASTA in the Wisconsin Genetics Software Package, Genetics Computer Group (GCG), 575 Science Dr., Madison, WI), or by inspection.

One preferred example of algorithms that are suitable for determining percent sequence identity and sequence similarity are the BLAST and BLAST 2.0 algorithms, which are described in Altschul et al. (1977) *Nucl. Acids Res.* 25:3389-3402 and Altschul et al. (1990) *J. Mol. Biol.* 215:403-410, respectively. BLAST and BLAST 2.0 can be used, for example with the parameters described herein, to determine percent

sequence identity for the polynucleotides of the invention. Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information. In one illustrative example, cumulative scores can be calculated using, for nucleotide sequences, the parameters M (reward score for a pair of matching residues; always >0) and N (penalty score for mismatching residues; always <0). Extension of the word hits in each direction are halted when: the cumulative alignment score falls off by the quantity X from its maximum achieved value; the cumulative score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments; or the end of either sequence is reached. The BLAST algorithm parameters W, T and X determine the sensitivity and speed of the alignment. The BLASTN program (for nucleotide sequences) uses as defaults a wordlength (W) of 11, and expectation (E) of 10, and the BLOSUM62 scoring matrix (see Henikoff and Henikoff (1989) *Proc. Natl. Acad. Sci. USA* 89:10915) alignments, (B) of 50, expectation (E) of 10, M=5, N=-4 and a comparison of both strands.

Preferably, the "percentage of sequence identity" is determined by comparing two optimally aligned sequences over a window of comparison of at least 20 positions, wherein the portion of the polynucleotide sequence in the comparison window may comprise additions or deletions (*i.e.*, gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference sequences (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical nucleic acid bases occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (*i.e.*, the window size) and multiplying the results by 100 to yield the percentage of sequence identity.

It will be appreciated by those of ordinary skill in the art that, as a result of the degeneracy of the genetic code, there are many nucleotide sequences that encode a polypeptide as described herein. Some of these polynucleotides bear minimal homology to the nucleotide sequence of any native gene. Nonetheless, polynucleotides that vary due to differences in codon usage are specifically contemplated by the present



invention. Further, alleles of the genes comprising the polynucleotide sequences provided herein are within the scope of the present invention. Alleles are endogenous genes that are altered as a result of one or more mutations, such as deletions, additions and/or substitutions of nucleotides. The resulting mRNA and protein may, but need not, have an altered structure or function. Alleles may be identified using standard techniques (such as hybridization, amplification and/or database sequence comparison).

Therefore, in another embodiment of the invention, a mutagenesis approach, such as site-specific mutagenesis, is employed for the preparation of immunogenic variants and/or derivatives of the polypeptides described herein. By this approach, specific modifications in a polypeptide sequence can be made through mutagenesis of the underlying polynucleotides that encode them. These techniques provides a straightforward approach to prepare and test sequence variants, for example, incorporating one or more of the foregoing considerations, by introducing one or more nucleotide sequence changes into the polynucleotide.

Site-specific mutagenesis allows the production of mutants through the use of specific oligonucleotide sequences which encode the DNA sequence of the desired mutation, as well as a sufficient number of adjacent nucleotides, to provide a primer sequence of sufficient size and sequence complexity to form a stable duplex on both sides of the deletion junction being traversed. Mutations may be employed in a selected polynucleotide sequence to improve, alter, decrease, modify, or otherwise change the properties of the polynucleotide itself, and/or alter the properties, activity, composition, stability, or primary sequence of the encoded polypeptide.

In certain embodiments of the present invention, the inventors contemplate the mutagenesis of the disclosed polynucleotide sequences to alter one or more properties of the encoded polypeptide, such as the immunogenicity of a polypeptide vaccine. The techniques of site-specific mutagenesis are well-known in the art, and are widely used to create variants of both polypeptides and polynucleotides. For example, site-specific mutagenesis is often used to alter a specific portion of a DNA molecule. In such embodiments, a primer comprising typically about 14 to about 25

nucleotides or so in length is employed, with about 5 to about 10 residues on both sides of the junction of the sequence being altered.

As will be appreciated by those of skill in the art, site-specific mutagenesis techniques have often employed a phage vector that exists in both a single  
5 stranded and double stranded form. Typical vectors useful in site-directed mutagenesis include vectors such as the M13 phage. These phage are readily commercially-available and their use is generally well-known to those skilled in the art. Double-stranded plasmids are also routinely employed in site directed mutagenesis that eliminates the step of transferring the gene of interest from a plasmid to a phage.

10 In general, site-directed mutagenesis in accordance herewith is performed by first obtaining a single-stranded vector or melting apart of two strands of a double-stranded vector that includes within its sequence a DNA sequence that encodes the desired peptide. An oligonucleotide primer bearing the desired mutated sequence is prepared, generally synthetically. This primer is then annealed with the single-stranded  
15 vector, and subjected to DNA polymerizing enzymes such as *E. coli* polymerase I Klenow fragment, in order to complete the synthesis of the mutation-bearing strand. Thus, a heteroduplex is formed wherein one strand encodes the original non-mutated sequence and the second strand bears the desired mutation. This heteroduplex vector is then used to transform appropriate cells, such as *E. coli* cells, and clones are selected  
20 which include recombinant vectors bearing the mutated sequence arrangement.

The preparation of sequence variants of the selected peptide-encoding DNA segments using site-directed mutagenesis provides a means of producing potentially useful species and is not meant to be limiting as there are other ways in which sequence variants of peptides and the DNA sequences encoding them may be  
25 obtained. For example, recombinant vectors encoding the desired peptide sequence may be treated with mutagenic agents, such as hydroxylamine, to obtain sequence variants. Specific details regarding these methods and protocols are found in the teachings of Maloy *et al.*, 1994; Segal, 1976; Prokop and Bajpai, 1991; Kuby, 1994; and Maniatis *et al.*, 1982, each incorporated herein by reference, for that purpose.

As used herein, the term "oligonucleotide directed mutagenesis procedure" refers to template-dependent processes and vector-mediated propagation which result in an increase in the concentration of a specific nucleic acid molecule relative to its initial concentration, or in an increase in the concentration of a detectable signal, such as amplification. As used herein, the term "oligonucleotide directed mutagenesis procedure" is intended to refer to a process that involves the template-dependent extension of a primer molecule. The term template dependent process refers to nucleic acid synthesis of an RNA or a DNA molecule wherein the sequence of the newly synthesized strand of nucleic acid is dictated by the well-known rules of complementary base pairing (see, for example, Watson, 1987). Typically, vector mediated methodologies involve the introduction of the nucleic acid fragment into a DNA or RNA vector, the clonal amplification of the vector, and the recovery of the amplified nucleic acid fragment. Examples of such methodologies are provided by U. S. Patent No. 4,237,224, specifically incorporated herein by reference in its entirety.

In another approach for the production of polypeptide variants of the present invention, recursive sequence recombination, as described in U.S. Patent No. 5,837,458, may be employed. In this approach, iterative cycles of recombination and screening or selection are performed to "evolve" individual polynucleotide variants of the invention having, for example, enhanced immunogenic activity.

In other embodiments of the present invention, the polynucleotide sequences provided herein can be advantageously used as probes or primers for nucleic acid hybridization. As such, it is contemplated that nucleic acid segments that comprise a sequence region of at least about 15 contiguous nucleotides that has the same sequence as, or is complementary to, a 15 nucleotide long contiguous sequence disclosed herein will find particular utility. Longer contiguous identical or complementary sequences, *e.g.*, those of about 20, 30, 40, 50, 100, 200, 500, 1000 (including all intermediate lengths) and even up to full length sequences will also be of use in certain embodiments.

The ability of such nucleic acid probes to specifically hybridize to a sequence of interest will enable them to be of use in detecting the presence of

complementary sequences in a given sample. However, other uses are also envisioned, such as the use of the sequence information for the preparation of mutant species primers, or primers for use in preparing other genetic constructions.

Polynucleotide molecules having sequence regions consisting of  
5 contiguous nucleotide stretches of 10-14, 15-20, 30, 50, or even of 100-200 nucleotides or so (including intermediate lengths as well), identical or complementary to a polynucleotide sequence disclosed herein, are particularly contemplated as hybridization probes for use in, *e.g.*, Southern and Northern blotting. This would allow a gene product, or fragment thereof, to be analyzed, both in diverse cell types and also in  
10 various bacterial cells. The total size of fragment, as well as the size of the complementary stretch(es), will ultimately depend on the intended use or application of the particular nucleic acid segment. Smaller fragments will generally find use in hybridization embodiments, wherein the length of the contiguous complementary region may be varied, such as between about 15 and about 100 nucleotides, but larger  
15 contiguous complementarity stretches may be used, according to the length complementary sequences one wishes to detect.

The use of a hybridization probe of about 15-25 nucleotides in length allows the formation of a duplex molecule that is both stable and selective. Molecules having contiguous complementary sequences over stretches greater than 15 bases in  
20 length are generally preferred, though, in order to increase stability and selectivity of the hybrid, and thereby improve the quality and degree of specific hybrid molecules obtained. One will generally prefer to design nucleic acid molecules having gene-complementary stretches of 15 to 25 contiguous nucleotides, or even longer where desired.

25 Hybridization probes may be selected from any portion of any of the sequences disclosed herein. All that is required is to review the sequences set forth herein, or to any continuous portion of the sequences, from about 15-25 nucleotides in length up to and including the full length sequence, that one wishes to utilize as a probe or primer. The choice of probe and primer sequences may be governed by various

factors. For example, one may wish to employ primers from towards the termini of the total sequence.

Small polynucleotide segments or fragments may be readily prepared by, for example, directly synthesizing the fragment by chemical means, as is commonly practiced using an automated oligonucleotide synthesizer. Also, fragments may be obtained by application of nucleic acid reproduction technology, such as the PCR™ technology of U. S. Patent 4,683,202 (incorporated herein by reference), by introducing selected sequences into recombinant vectors for recombinant production, and by other recombinant DNA techniques generally known to those of skill in the art of molecular biology.

The nucleotide sequences of the invention may be used for their ability to selectively form duplex molecules with complementary stretches of the entire gene or gene fragments of interest. Depending on the application envisioned, one will typically desire to employ varying conditions of hybridization to achieve varying degrees of selectivity of probe towards target sequence. For applications requiring high selectivity, one will typically desire to employ relatively stringent conditions to form the hybrids, *e.g.*, one will select relatively low salt and/or high temperature conditions, such as provided by a salt concentration of from about 0.02 M to about 0.15 M salt at temperatures of from about 50°C to about 70°C. Such selective conditions tolerate little, if any, mismatch between the probe and the template or target strand, and would be particularly suitable for isolating related sequences.

Of course, for some applications, for example, where one desires to prepare mutants employing a mutant primer strand hybridized to an underlying template, less stringent (reduced stringency) hybridization conditions will typically be needed in order to allow formation of the heteroduplex. In these circumstances, one may desire to employ salt conditions such as those of from about 0.15 M to about 0.9 M salt, at temperatures ranging from about 20°C to about 55°C. Cross-hybridizing species can thereby be readily identified as positively hybridizing signals with respect to control hybridizations. In any case, it is generally appreciated that conditions can be rendered more stringent by the addition of increasing amounts of formamide, which serves to

destabilize the hybrid duplex in the same manner as increased temperature. Thus, hybridization conditions can be readily manipulated, and thus will generally be a method of choice depending on the desired results.

According to another embodiment of the present invention, polynucleotide compositions comprising antisense oligonucleotides are provided. Antisense oligonucleotides have been demonstrated to be effective and targeted inhibitors of protein synthesis, and, consequently, provide a therapeutic approach by which a disease can be treated by inhibiting the synthesis of proteins that contribute to the disease. The efficacy of antisense oligonucleotides for inhibiting protein synthesis is well established. For example, the synthesis of polygalacturonase and the muscarine type 2 acetylcholine receptor are inhibited by antisense oligonucleotides directed to their respective mRNA sequences (U. S. Patent 5,739,119 and U. S. Patent 5,759,829). Further, examples of antisense inhibition have been demonstrated with the nuclear protein cyclin, the multiple drug resistance gene (MDG1), ICAM-1, E-selectin, STK-1, striatal GABA<sub>A</sub> receptor and human EGF (Jaskulski *et al.*, Science. 1988 Jun 10;240(4858):1544-6; Vasanthakumar and Ahmed, Cancer Commun. 1989;1(4):225-32; Peris *et al.*, Brain Res Mol Brain Res. 1998 Jun 15;57(2):310-20; U. S. Patent 5,801,154; U.S. Patent 5,789,573; U. S. Patent 5,718,709 and U.S. Patent 5,610,288). Antisense constructs have also been described that inhibit and can be used to treat a variety of abnormal cellular proliferations, *e.g.* cancer (U. S. Patent 5,747,470; U. S. Patent 5,591,317 and U. S. Patent 5,783,683).

Therefore, in certain embodiments, the present invention provides oligonucleotide sequences that comprise all, or a portion of, any sequence that is capable of specifically binding to polynucleotide sequence described herein, or a complement thereof. In one embodiment, the antisense oligonucleotides comprise DNA or derivatives thereof. In another embodiment, the oligonucleotides comprise RNA or derivatives thereof. In a third embodiment, the oligonucleotides are modified DNAs comprising a phosphorothioated modified backbone. In a fourth embodiment, the oligonucleotide sequences comprise peptide nucleic acids or derivatives thereof. In each case, preferred compositions comprise a sequence region that is complementary,

and more preferably substantially-complementary, and even more preferably, completely complementary to one or more portions of polynucleotides disclosed herein. Selection of antisense compositions specific for a given gene sequence is based upon analysis of the chosen target sequence and determination of secondary structure,  $T_m$ ,  
5 binding energy, and relative stability. Antisense compositions may be selected based upon their relative inability to form dimers, hairpins, or other secondary structures that would reduce or prohibit specific binding to the target mRNA in a host cell. Highly preferred target regions of the mRNA, are those which are at or near the AUG translation initiation codon, and those sequences which are substantially complementary  
10 to 5' regions of the mRNA. These secondary structure analyses and target site selection considerations can be performed, for example, using v.4 of the OLIGO primer analysis software and/or the BLASTN 2.0.5 algorithm software (Altschul *et al.*, Nucleic Acids Res. 1997 Sep 1;25(17):3389-402).

The use of an antisense delivery method employing a short peptide  
15 vector, termed MPG (27 residues), is also contemplated. The MPG peptide contains a hydrophobic domain derived from the fusion sequence of HIV gp41 and a hydrophilic domain from the nuclear localization sequence of SV40 T-antigen (Morris *et al.*, Nucleic Acids Res. 1997 Jul 15;25(14):2730-6). It has been demonstrated that several molecules of the MPG peptide coat the antisense oligonucleotides and can be delivered  
20 into cultured mammalian cells in less than 1 hour with relatively high efficiency (90%). Further, the interaction with MPG strongly increases both the stability of the oligonucleotide to nuclease and the ability to cross the plasma membrane.

According to another embodiment of the invention, the polynucleotide compositions described herein are used in the design and preparation of ribozyme  
25 molecules for inhibiting expression of the tumor polypeptides and proteins of the present invention in tumor cells. Ribozymes are RNA-protein complexes that cleave nucleic acids in a site-specific fashion. Ribozymes have specific catalytic domains that possess endonuclease activity (Kim and Cech, Proc Natl Acad Sci U S A. 1987 Dec;84(24):8788-92; Forster and Symons, Cell. 1987 Apr 24;49(2):211-20). For  
30 example, a large number of ribozymes accelerate phosphoester transfer reactions with a

high degree of specificity, often cleaving only one of several phosphoesters in an oligonucleotide substrate (Cech *et al.*, Cell. 1981 Dec;27(3 Pt 2):487-96; Michel and Westhof, J Mol Biol. 1990 Dec 5;216(3):585-610; Reinhold-Hurek and Shub, Nature. 1992 May 14;357(6374):173-6). This specificity has been attributed to the requirement  
5 that the substrate bind via specific base-pairing interactions to the internal guide sequence ("IGS") of the ribozyme prior to chemical reaction.

Six basic varieties of naturally-occurring enzymatic RNAs are known presently. Each can catalyze the hydrolysis of RNA phosphodiester bonds *in trans* (and thus can cleave other RNA molecules) under physiological conditions. In general,  
10 enzymatic nucleic acids act by first binding to a target RNA. Such binding occurs through the target binding portion of a enzymatic nucleic acid which is held in close proximity to an enzymatic portion of the molecule that acts to cleave the target RNA. Thus, the enzymatic nucleic acid first recognizes and then binds a target RNA through complementary base-pairing, and once bound to the correct site, acts enzymatically to  
15 cut the target RNA. Strategic cleavage of such a target RNA will destroy its ability to direct synthesis of an encoded protein. After an enzymatic nucleic acid has bound and cleaved its RNA target, it is released from that RNA to search for another target and can repeatedly bind and cleave new targets.

The enzymatic nature of a ribozyme is advantageous over many  
20 technologies, such as antisense technology (where a nucleic acid molecule simply binds to a nucleic acid target to block its translation) since the concentration of ribozyme necessary to affect a therapeutic treatment is lower than that of an antisense oligonucleotide. This advantage reflects the ability of the ribozyme to act enzymatically. Thus, a single ribozyme molecule is able to cleave many molecules of  
25 target RNA. In addition, the ribozyme is a highly specific inhibitor, with the specificity of inhibition depending not only on the base pairing mechanism of binding to the target RNA, but also on the mechanism of target RNA cleavage. Single mismatches, or base-substitutions, near the site of cleavage can completely eliminate catalytic activity of a ribozyme. Similar mismatches in antisense molecules do not prevent their action  
30 (Woelf *et al.*, Proc Natl Acad Sci U S A. 1992 Aug 15;89(16):7305-9). Thus, the



specificity of action of a ribozyme is greater than that of an antisense oligonucleotide binding the same RNA site.

The enzymatic nucleic acid molecule may be formed in a hammerhead, hairpin, a hepatitis  $\delta$  virus, group I intron or RNaseP RNA (in association with an RNA  
5 guide sequence) or Neurospora VS RNA motif. Examples of hammerhead motifs are described by Rossi *et al.* Nucleic Acids Res. 1992 Sep 11;20(17):4559-65. Examples of hairpin motifs are described by Hampel *et al.* (Eur. Pat. Appl. Publ. No. EP 0360257), Hampel and Tritz, Biochemistry 1989 Jun 13;28(12):4929-33; Hampel *et al.*, Nucleic  
10 Acids Res. 1990 Jan 25;18(2):299-304 and U. S. Patent 5,631,359. An example of the hepatitis  $\delta$  virus motif is described by Perrotta and Been, Biochemistry. 1992 Dec 1;31(47):11843-52; an example of the RNaseP motif is described by Guerrier-Takada  
*et al.*, Cell. 1983 Dec;35(3 Pt 2):849-57; Neurospora VS RNA ribozyme motif is described by Collins (Saville and Collins, Cell. 1990 May 18;61(4):685-96; Saville and  
15 Collins, Proc Natl Acad Sci U S A. 1991 Oct 1;88(19):8826-30; Collins and Olive, Biochemistry. 1993 Mar 23;32(11):2795-9); and an example of the Group I intron is described in (U. S. Patent 4,987,071). All that is important in an enzymatic nucleic acid  
molecule of this invention is that it has a specific substrate binding site which is complementary to one or more of the target gene RNA regions, and that it have  
nucleotide sequences within or surrounding that substrate binding site which impart an  
20 RNA cleaving activity to the molecule. Thus the ribozyme constructs need not be limited to specific motifs mentioned herein.

Ribozymes may be designed as described in Int. Pat. Appl. Publ. No. WO 93/23569 and Int. Pat. Appl. Publ. No. WO 94/02595, each specifically  
incorporated herein by reference) and synthesized to be tested *in vitro* and *in vivo*, as  
25 described. Such ribozymes can also be optimized for delivery. While specific examples are provided, those in the art will recognize that equivalent RNA targets in other species can be utilized when necessary.

Ribozyme activity can be optimized by altering the length of the ribozyme binding arms, or chemically synthesizing ribozymes with modifications that  
30 prevent their degradation by serum ribonucleases (see *e.g.*, Int. Pat. Appl. Publ. No. WO

92/07065; Int. Pat. Appl. Publ. No. WO 93/15187; Int. Pat. Appl. Publ. No. WO 91/03162; Eur. Pat. Appl. Publ. No. 92110298.4; U. S. Patent 5,334,711; and Int. Pat. Appl. Publ. No. WO 94/13688, which describe various chemical modifications that can be made to the sugar moieties of enzymatic RNA molecules), modifications which enhance their efficacy in cells, and removal of stem II bases to shorten RNA synthesis times and reduce chemical requirements.

Sullivan *et al.* (Int. Pat. Appl. Publ. No. WO 94/02595) describes the general methods for delivery of enzymatic RNA molecules. Ribozymes may be administered to cells by a variety of methods known to those familiar to the art, including, but not restricted to, encapsulation in liposomes, by iontophoresis, or by incorporation into other vehicles, such as hydrogels, cyclodextrins, biodegradable nanocapsules, and bioadhesive microspheres. For some indications, ribozymes may be directly delivered *ex vivo* to cells or tissues with or without the aforementioned vehicles. Alternatively, the RNA/vehicle combination may be locally delivered by direct inhalation, by direct injection or by use of a catheter, infusion pump or stent. Other routes of delivery include, but are not limited to, intravascular, intramuscular, subcutaneous or joint injection, aerosol inhalation, oral (tablet or pill form), topical, systemic, ocular, intraperitoneal and/or intrathecal delivery. More detailed descriptions of ribozyme delivery and administration are provided in Int. Pat. Appl. Publ. No. WO 94/02595 and Int. Pat. Appl. Publ. No. WO 93/23569, each specifically incorporated herein by reference.

Another means of accumulating high concentrations of a ribozyme(s) within cells is to incorporate the ribozyme-encoding sequences into a DNA expression vector. Transcription of the ribozyme sequences are driven from a promoter for eukaryotic RNA polymerase I (pol I), RNA polymerase II (pol II), or RNA polymerase III (pol III). Transcripts from pol II or pol III promoters will be expressed at high levels in all cells; the levels of a given pol II promoter in a given cell type will depend on the nature of the gene regulatory sequences (enhancers, silencers, *etc.*) present nearby. Prokaryotic RNA polymerase promoters may also be used, providing that the prokaryotic RNA polymerase enzyme is expressed in the appropriate cells. Ribozymes

expressed from such promoters have been shown to function in mammalian cells. Such transcription units can be incorporated into a variety of vectors for introduction into mammalian cells, including but not restricted to, plasmid DNA vectors, viral DNA vectors (such as adenovirus or adeno-associated vectors), or viral RNA vectors (such as  
5 retroviral, semliki forest virus, sindbis virus vectors).

In another embodiment of the invention, peptide nucleic acids (PNAs) compositions are provided. PNA is a DNA mimic in which the nucleobases are attached to a pseudopeptide backbone (Good and Nielsen, *Antisense Nucleic Acid Drug Dev.* 1997 7(4) 431-37). PNA is able to be utilized in a number methods that  
10 traditionally have used RNA or DNA. Often PNA sequences perform better in techniques than the corresponding RNA or DNA sequences and have utilities that are not inherent to RNA or DNA. A review of PNA including methods of making, characteristics of, and methods of using, is provided by Corey (*Trends Biotechnol* 1997 Jun;15(6):224-9). As such, in certain embodiments, one may prepare PNA sequences  
15 that are complementary to one or more portions of the ACE mRNA sequence, and such PNA compositions may be used to regulate, alter, decrease, or reduce the translation of ACE-specific mRNA, and thereby alter the level of ACE activity in a host cell to which such PNA compositions have been administered.

PNAs have 2-aminoethyl-glycine linkages replacing the normal  
20 phosphodiester backbone of DNA (Nielsen *et al.*, *Science* 1991 Dec 6;254(5037):1497-500; Hanvey *et al.*, *Science*. 1992 Nov 27;258(5087):1481-5; Hyrup and Nielsen, *Bioorg Med Chem.* 1996 Jan;4(1):5-23). This chemistry has three important consequences: firstly, in contrast to DNA or phosphorothioate oligonucleotides, PNAs are neutral molecules; secondly, PNAs are achiral, which avoids the need to develop a  
25 stereoselective synthesis; and thirdly, PNA synthesis uses standard Boc or Fmoc protocols for solid-phase peptide synthesis, although other methods, including a modified Merrifield method, have been used.

PNA monomers or ready-made oligomers are commercially available from PerSeptive Biosystems (Framingham, MA). PNA syntheses by either Boc or  
30 Fmoc protocols are straightforward using manual or automated protocols (Norton *et al.*,

Bioorg Med Chem. 1995 Apr;3(4):437-45). The manual protocol lends itself to the production of chemically modified PNAs or the simultaneous synthesis of families of closely related PNAs.

As with peptide synthesis, the success of a particular PNA synthesis will  
5 depend on the properties of the chosen sequence. For example, while in theory PNAs can incorporate any combination of nucleotide bases, the presence of adjacent purines can lead to deletions of one or more residues in the product. In expectation of this difficulty, it is suggested that, in producing PNAs with adjacent purines, one should repeat the coupling of residues likely to be added inefficiently. This should be followed  
10 by the purification of PNAs by reverse-phase high-pressure liquid chromatography, providing yields and purity of product similar to those observed during the synthesis of peptides.

Modifications of PNAs for a given application may be accomplished by coupling amino acids during solid-phase synthesis or by attaching compounds that  
15 contain a carboxylic acid group to the exposed N-terminal amine. Alternatively, PNAs can be modified after synthesis by coupling to an introduced lysine or cysteine. The ease with which PNAs can be modified facilitates optimization for better solubility or for specific functional requirements. Once synthesized, the identity of PNAs and their derivatives can be confirmed by mass spectrometry. Several studies have made and  
20 utilized modifications of PNAs (for example, Norton *et al.*, Bioorg Med Chem. 1995 Apr;3(4):437-45; Petersen *et al.*, J Pept Sci. 1995 May-Jun;1(3):175-83; Orum *et al.*, Biotechniques. 1995 Sep;19(3):472-80; Footer *et al.*, Biochemistry. 1996 Aug 20;35(33):10673-9; Griffith *et al.*, Nucleic Acids Res. 1995 Aug 11;23(15):3003-8; Pardridge *et al.*, Proc Natl Acad Sci U S A. 1995 Jun 6;92(12):5592-6; Boffa *et al.*,  
25 Proc Natl Acad Sci U S A. 1995 Mar 14;92(6):1901-5; Gambacorti-Passerini *et al.*, Blood. 1996 Aug 15;88(4):1411-7; Armitage *et al.*, Proc Natl Acad Sci U S A. 1997 Nov 11;94(23):12320-5; Seeger *et al.*, Biotechniques. 1997 Sep;23(3):512-7). U.S. Patent No. 5,700,922 discusses PNA-DNA-PNA chimeric molecules and their uses in diagnostics, modulating protein in organisms, and treatment of conditions susceptible to  
30 therapeutics.

Methods of characterizing the antisense binding properties of PNAs are discussed in Rose (Anal Chem. 1993 Dec 15;65(24):3545-9) and Jensen *et al.* (Biochemistry. 1997 Apr 22;36(16):5072-7). Rose uses capillary gel electrophoresis to determine binding of PNAs to their complementary oligonucleotide, measuring the relative binding kinetics and stoichiometry. Similar types of measurements were made by Jensen *et al.* using BIAcore™ technology.

Other applications of PNAs that have been described and will be apparent to the skilled artisan include use in DNA strand invasion, antisense inhibition, mutational analysis, enhancers of transcription, nucleic acid purification, isolation of transcriptionally active genes, blocking of transcription factor binding, genome cleavage, biosensors, *in situ* hybridization, and the like.

#### Polynucleotide Identification, Characterization and Expression

Polynucleotide compositions of the present invention may be identified, prepared and/or manipulated using any of a variety of well established techniques (see generally, Sambrook *et al.*, *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989, and other like references). For example, a polynucleotide may be identified, as described in more detail below, by screening a microarray of cDNAs for tumor-associated expression (*i.e.*, expression that is at least two fold greater in a tumor than in normal tissue, as determined using a representative assay provided herein). Such screens may be performed, for example, using the microarray technology of Affymetrix, Inc. (Santa Clara, CA) according to the manufacturer's instructions (and essentially as described by Schena *et al.*, *Proc. Natl. Acad. Sci. USA* 93:10614-10619, 1996 and Heller *et al.*, *Proc. Natl. Acad. Sci. USA* 94:2150-2155, 1997). Alternatively, polynucleotides may be amplified from cDNA prepared from cells expressing the proteins described herein, such as tumor cells.

Many template dependent processes are available to amplify a target sequences of interest present in a sample. One of the best known amplification methods is the polymerase chain reaction (PCR™) which is described in detail in U.S. Patent Nos. 4,683,195, 4,683,202 and 4,800,159, each of which is incorporated herein by

reference in its entirety. Briefly, in PCR™, two primer sequences are prepared which are complementary to regions on opposite complementary strands of the target sequence. An excess of deoxynucleoside triphosphates is added to a reaction mixture along with a DNA polymerase (*e.g.*, *Taq* polymerase). If the target sequence is present  
5 in a sample, the primers will bind to the target and the polymerase will cause the primers to be extended along the target sequence by adding on nucleotides. By raising and lowering the temperature of the reaction mixture, the extended primers will dissociate from the target to form reaction products, excess primers will bind to the target and to the reaction product and the process is repeated. Preferably reverse  
10 transcription and PCR™ amplification procedure may be performed in order to quantify the amount of mRNA amplified. Polymerase chain reaction methodologies are well known in the art.

Any of a number of other template dependent processes, many of which are variations of the PCR™ amplification technique, are readily known and available in  
15 the art. Illustratively, some such methods include the ligase chain reaction (referred to as LCR), described, for example, in Eur. Pat. Appl. Publ. No. 320,308 and U.S. Patent No. 4,883,750; Qbeta Replicase, described in PCT Intl. Pat. Appl. Publ. No. PCT/US87/00880; Strand Displacement Amplification (SDA) and Repair Chain Reaction (RCR). Still other amplification methods are described in Great Britain Pat.  
20 Appl. No. 2 202 328, and in PCT Intl. Pat. Appl. Publ. No. PCT/US89/01025. Other nucleic acid amplification procedures include transcription-based amplification systems (TAS) (PCT Intl. Pat. Appl. Publ. No. WO 88/10315), including nucleic acid sequence based amplification (NASBA) and 3SR. Eur. Pat. Appl. Publ. No. 329,822 describes a nucleic acid amplification process involving cyclically synthesizing single-stranded  
25 RNA ("ssRNA"), ssDNA, and double-stranded DNA (dsDNA). PCT Intl. Pat. Appl. Publ. No. WO 89/06700 describes a nucleic acid sequence amplification scheme based on the hybridization of a promoter/primer sequence to a target single-stranded DNA ("ssDNA") followed by transcription of many RNA copies of the sequence. Other amplification methods such as "RACE" (Frohman, 1990), and "one-sided PCR" (Ohara,  
30 1989) are also well-known to those of skill in the art.

An amplified portion of a polynucleotide of the present invention may be used to isolate a full length gene from a suitable library (e.g., a tumor cDNA library) using well known techniques. Within such techniques, a library (cDNA or genomic) is screened using one or more polynucleotide probes or primers suitable for amplification.

5 Preferably, a library is size-selected to include larger molecules. Random primed libraries may also be preferred for identifying 5' and upstream regions of genes. Genomic libraries are preferred for obtaining introns and extending 5' sequences.

For hybridization techniques, a partial sequence may be labeled (e.g., by nick-translation or end-labeling with  $^{32}\text{P}$ ) using well known techniques. A bacterial or bacteriophage library is then generally screened by hybridizing filters containing denatured bacterial colonies (or lawns containing phage plaques) with the labeled probe (see Sambrook et al., *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989). Hybridizing colonies or plaques are selected and expanded, and the DNA is isolated for further analysis. cDNA clones may

10 be analyzed to determine the amount of additional sequence by, for example, PCR using a primer from the partial sequence and a primer from the vector. Restriction maps and partial sequences may be generated to identify one or more overlapping clones. The complete sequence may then be determined using standard techniques, which may involve generating a series of deletion clones. The resulting overlapping sequences can

15 then assembled into a single contiguous sequence. A full length cDNA molecule can be generated by ligating suitable fragments, using well known techniques.

Alternatively, amplification techniques, such as those described above, can be useful for obtaining a full length coding sequence from a partial cDNA sequence. One such amplification technique is inverse PCR (see Triglia et al., *Nucl. Acids Res.*

25 16:8186, 1988), which uses restriction enzymes to generate a fragment in the known region of the gene. The fragment is then circularized by intramolecular ligation and used as a template for PCR with divergent primers derived from the known region. Within an alternative approach, sequences adjacent to a partial sequence may be retrieved by amplification with a primer to a linker sequence and a primer specific to a

30 known region. The amplified sequences are typically subjected to a second round of

amplification with the same linker primer and a second primer specific to the known region. A variation on this procedure, which employs two primers that initiate extension in opposite directions from the known sequence, is described in WO 96/38591. Another such technique is known as "rapid amplification of cDNA ends" or  
5 RACE. This technique involves the use of an internal primer and an external primer, which hybridizes to a polyA region or vector sequence, to identify sequences that are 5' and 3' of a known sequence. Additional techniques include capture PCR (Lagerstrom et al., *PCR Methods Applic.* 1:111-19, 1991) and walking PCR (Parker et al., *Nucl. Acids. Res.* 19:3055-60, 1991). Other methods employing amplification may also be employed  
10 to obtain a full length cDNA sequence.

In certain instances, it is possible to obtain a full length cDNA sequence by analysis of sequences provided in an expressed sequence tag (EST) database, such as that available from GenBank. Searches for overlapping ESTs may generally be performed using well known programs (e.g., NCBI BLAST searches), and such ESTs  
15 may be used to generate a contiguous full length sequence. Full length DNA sequences may also be obtained by analysis of genomic fragments.

In other embodiments of the invention, polynucleotide sequences or fragments thereof which encode polypeptides of the invention, or fusion proteins or functional equivalents thereof, may be used in recombinant DNA molecules to direct  
20 expression of a polypeptide in appropriate host cells. Due to the inherent degeneracy of the genetic code, other DNA sequences that encode substantially the same or a functionally equivalent amino acid sequence may be produced and these sequences may be used to clone and express a given polypeptide.

As will be understood by those of skill in the art, it may be advantageous  
25 in some instances to produce polypeptide-encoding nucleotide sequences possessing non-naturally occurring codons. For example, codons preferred by a particular prokaryotic or eukaryotic host can be selected to increase the rate of protein expression or to produce a recombinant RNA transcript having desirable properties, such as a half-life which is longer than that of a transcript generated from the naturally occurring  
30 sequence.



Moreover, the polynucleotide sequences of the present invention can be engineered using methods generally known in the art in order to alter polypeptide encoding sequences for a variety of reasons, including but not limited to, alterations which modify the cloning, processing, and/or expression of the gene product. For example, DNA shuffling by random fragmentation and PCR reassembly of gene fragments and synthetic oligonucleotides may be used to engineer the nucleotide sequences. In addition, site-directed mutagenesis may be used to insert new restriction sites, alter glycosylation patterns, change codon preference, produce splice variants, or introduce mutations, and so forth.

In another embodiment of the invention, natural, modified, or recombinant nucleic acid sequences may be ligated to a heterologous sequence to encode a fusion protein. For example, to screen peptide libraries for inhibitors of polypeptide activity, it may be useful to encode a chimeric protein that can be recognized by a commercially available antibody. A fusion protein may also be engineered to contain a cleavage site located between the polypeptide-encoding sequence and the heterologous protein sequence, so that the polypeptide may be cleaved and purified away from the heterologous moiety.

Sequences encoding a desired polypeptide may be synthesized, in whole or in part, using chemical methods well known in the art (see Caruthers, M. H. et al. (1980) *Nucl. Acids Res. Symp. Ser.* 215-223, Horn, T. et al. (1980) *Nucl. Acids Res. Symp. Ser.* 225-232). Alternatively, the protein itself may be produced using chemical methods to synthesize the amino acid sequence of a polypeptide, or a portion thereof. For example, peptide synthesis can be performed using various solid-phase techniques (Roberge, J. Y. et al. (1995) *Science* 269:202-204) and automated synthesis may be achieved, for example, using the ABI 431A Peptide Synthesizer (Perkin Elmer, Palo Alto, CA).

A newly synthesized peptide may be substantially purified by preparative high performance liquid chromatography (e.g., Creighton, T. (1983) *Proteins, Structures and Molecular Principles*, WH Freeman and Co., New York, N.Y.) or other comparable techniques available in the art. The composition of the synthetic peptides may be

confirmed by amino acid analysis or sequencing (e.g., the Edman degradation procedure). Additionally, the amino acid sequence of a polypeptide, or any part thereof, may be altered during direct synthesis and/or combined using chemical methods with sequences from other proteins, or any part thereof, to produce a variant polypeptide.

5           In order to express a desired polypeptide, the nucleotide sequences encoding the polypeptide, or functional equivalents, may be inserted into appropriate expression vector, *i.e.*, a vector which contains the necessary elements for the transcription and translation of the inserted coding sequence. Methods which are well known to those skilled in the art may be used to construct expression vectors containing  
10 sequences encoding a polypeptide of interest and appropriate transcriptional and translational control elements. These methods include *in vitro* recombinant DNA techniques, synthetic techniques, and *in vivo* genetic recombination. Such techniques are described, for example, in Sambrook, J. et al. (1989) *Molecular Cloning, A Laboratory Manual*, Cold Spring Harbor Press, Plainview, N.Y., and Ausubel, F. M. et  
15 al. (1989) *Current Protocols in Molecular Biology*, John Wiley & Sons, New York. N.Y.

A variety of expression vector/host systems may be utilized to contain and express polynucleotide sequences. These include, but are not limited to, microorganisms such as bacteria transformed with recombinant bacteriophage, plasmid,  
20 or cosmid DNA expression vectors; yeast transformed with yeast expression vectors; insect cell systems infected with virus expression vectors (e.g., baculovirus); plant cell systems transformed with virus expression vectors (e.g., cauliflower mosaic virus, CaMV; tobacco mosaic virus, TMV) or with bacterial expression vectors (e.g., Ti or pBR322 plasmids); or animal cell systems.

25           The "control elements" or "regulatory sequences" present in an expression vector are those non-translated regions of the vector--enhancers, promoters, 5' and 3' untranslated regions--which interact with host cellular proteins to carry out transcription and translation. Such elements may vary in their strength and specificity. Depending on the vector system and host utilized, any number of suitable transcription  
30 and translation elements, including constitutive and inducible promoters, may be used.

For example, when cloning in bacterial systems, inducible promoters such as the hybrid lacZ promoter of the PBLUESCRIPT phagemid (Stratagene, La Jolla, Calif.) or PSPORT1 plasmid (Gibco BRL, Gaithersburg, MD) and the like may be used. In mammalian cell systems, promoters from mammalian genes or from mammalian viruses are generally preferred. If it is necessary to generate a cell line that contains multiple copies of the sequence encoding a polypeptide, vectors based on SV40 or EBV may be advantageously used with an appropriate selectable marker.

In bacterial systems, any of a number of expression vectors may be selected depending upon the use intended for the expressed polypeptide. For example, when large quantities are needed, for example for the induction of antibodies, vectors which direct high level expression of fusion proteins that are readily purified may be used. Such vectors include, but are not limited to, the multifunctional *E. coli* cloning and expression vectors such as BLUESCRIPT (Stratagene), in which the sequence encoding the polypeptide of interest may be ligated into the vector in frame with sequences for the amino-terminal Met and the subsequent 7 residues of .beta.-galactosidase so that a hybrid protein is produced; pIN vectors (Van Heeke, G. and S. M. Schuster (1989) *J. Biol. Chem.* 264:5503-5509); and the like. pGEX Vectors (Promega, Madison, Wis.) may also be used to express foreign polypeptides as fusion proteins with glutathione S-transferase (GST). In general, such fusion proteins are soluble and can easily be purified from lysed cells by adsorption to glutathione-agarose beads followed by elution in the presence of free glutathione. Proteins made in such systems may be designed to include heparin, thrombin, or factor XA protease cleavage sites so that the cloned polypeptide of interest can be released from the GST moiety at will.

In the yeast, *Saccharomyces cerevisiae*, a number of vectors containing constitutive or inducible promoters such as alpha factor, alcohol oxidase, and PGH may be used. For reviews, see Ausubel et al. (supra) and Grant et al. (1987) *Methods Enzymol.* 153:516-544.

In cases where plant expression vectors are used, the expression of sequences encoding polypeptides may be driven by any of a number of promoters. For

example, viral promoters such as the 35S and 19S promoters of CaMV may be used alone or in combination with the omega leader sequence from TMV (Takamatsu, N. (1987) *EMBO J.* 6:307-311. Alternatively, plant promoters such as the small subunit of RUBISCO or heat shock promoters may be used (Coruzzi, G. et al. (1984) *EMBO J.* 3:1671-1680; Broglie, R. et al. (1984) *Science* 224:838-843; and Winter, J. et al. (1991) *Results Probl. Cell Differ.* 17:85-105). These constructs can be introduced into plant cells by direct DNA transformation or pathogen-mediated transfection. Such techniques are described in a number of generally available reviews (see, for example, Hobbs, S. or Murry, L. E. in McGraw Hill Yearbook of Science and Technology (1992) McGraw Hill, New York, N.Y.; pp. 191-196).

An insect system may also be used to express a polypeptide of interest. For example, in one such system, *Autographa californica* nuclear polyhedrosis virus (AcNPV) is used as a vector to express foreign genes in *Spodoptera frugiperda* cells or in *Trichoplusia* larvae. The sequences encoding the polypeptide may be cloned into a non-essential region of the virus, such as the polyhedrin gene, and placed under control of the polyhedrin promoter. Successful insertion of the polypeptide-encoding sequence will render the polyhedrin gene inactive and produce recombinant virus lacking coat protein. The recombinant viruses may then be used to infect, for example, *S. frugiperda* cells or *Trichoplusia* larvae in which the polypeptide of interest may be expressed (Engelhard, E. K. et al. (1994) *Proc. Natl. Acad. Sci.* 91:3224-3227).

In mammalian host cells, a number of viral-based expression systems are generally available. For example, in cases where an adenovirus is used as an expression vector, sequences encoding a polypeptide of interest may be ligated into an adenovirus transcription/translation complex consisting of the late promoter and tripartite leader sequence. Insertion in a non-essential E1 or E3 region of the viral genome may be used to obtain a viable virus which is capable of expressing the polypeptide in infected host cells (Logan, J. and Shenk, T. (1984) *Proc. Natl. Acad. Sci.* 81:3655-3659). In addition, transcription enhancers, such as the Rous sarcoma virus (RSV) enhancer, may be used to increase expression in mammalian host cells.

Specific initiation signals may also be used to achieve more efficient translation of sequences encoding a polypeptide of interest. Such signals include the ATG initiation codon and adjacent sequences. In cases where sequences encoding the polypeptide, its initiation codon, and upstream sequences are inserted into the appropriate expression vector, no additional transcriptional or translational control signals may be needed. However, in cases where only coding sequence, or a portion thereof, is inserted, exogenous translational control signals including the ATG initiation codon should be provided. Furthermore, the initiation codon should be in the correct reading frame to ensure translation of the entire insert. Exogenous translational elements and initiation codons may be of various origins, both natural and synthetic. The efficiency of expression may be enhanced by the inclusion of enhancers which are appropriate for the particular cell system which is used, such as those described in the literature (Scharf, D. et al. (1994) *Results Probl. Cell Differ.* 20:125-162).

In addition, a host cell strain may be chosen for its ability to modulate the expression of the inserted sequences or to process the expressed protein in the desired fashion. Such modifications of the polypeptide include, but are not limited to, acetylation, carboxylation, glycosylation, phosphorylation, lipidation, and acylation. Post-translational processing which cleaves a "prepro" form of the protein may also be used to facilitate correct insertion, folding and/or function. Different host cells such as CHO, COS, HeLa, MDCK, HEK293, and WI38, which have specific cellular machinery and characteristic mechanisms for such post-translational activities, may be chosen to ensure the correct modification and processing of the foreign protein.

For long-term, high-yield production of recombinant proteins, stable expression is generally preferred. For example, cell lines which stably express a polynucleotide of interest may be transformed using expression vectors which may contain viral origins of replication and/or endogenous expression elements and a selectable marker gene on the same or on a separate vector. Following the introduction of the vector, cells may be allowed to grow for 1-2 days in an enriched media before they are switched to selective media. The purpose of the selectable marker is to confer resistance to selection, and its presence allows growth and recovery of cells which

successfully express the introduced sequences. Resistant clones of stably transformed cells may be proliferated using tissue culture techniques appropriate to the cell type.

Any number of selection systems may be used to recover transformed cell lines. These include, but are not limited to, the herpes simplex virus thymidine kinase (Wigler, M. et al. (1977) *Cell* 11:223-32) and adenine phosphoribosyltransferase (Lowy, I. et al. (1990) *Cell* 22:817-23) genes which can be employed in tk.sup.- or apt.sup.- cells, respectively. Also, antimetabolite, antibiotic or herbicide resistance can be used as the basis for selection; for example, dhfr which confers resistance to methotrexate (Wigler, M. et al. (1980) *Proc. Natl. Acad. Sci.* 77:3567-70); npt, which confers resistance to the aminoglycosides, neomycin and G-418 (Colbere-Garapin, F. et al (1981) *J. Mol. Biol.* 150:1-14); and als or pat, which confer resistance to chlorsulfuron and phosphinotricin acetyltransferase, respectively (Murry, *supra*). Additional selectable genes have been described, for example, trpB, which allows cells to utilize indole in place of tryptophan, or hisD, which allows cells to utilize histinol in place of histidine (Hartman, S. C. and R. C. Mulligan (1988) *Proc. Natl. Acad. Sci.* 85:8047-51). The use of visible markers has gained popularity with such markers as anthocyanins, beta-glucuronidase and its substrate GUS, and luciferase and its substrate luciferin, being widely used not only to identify transformants, but also to quantify the amount of transient or stable protein expression attributable to a specific vector system (Rhodes, C. A. et al. (1995) *Methods Mol. Biol.* 55:121-131).

Although the presence/absence of marker gene expression suggests that the gene of interest is also present, its presence and expression may need to be confirmed. For example, if the sequence encoding a polypeptide is inserted within a marker gene sequence, recombinant cells containing sequences can be identified by the absence of marker gene function. Alternatively, a marker gene can be placed in tandem with a polypeptide-encoding sequence under the control of a single promoter. Expression of the marker gene in response to induction or selection usually indicates expression of the tandem gene as well.

Alternatively, host cells that contain and express a desired polynucleotide sequence may be identified by a variety of procedures known to those of

skill in the art. These procedures include, but are not limited to, DNA-DNA or DNA-RNA hybridizations and protein bioassay or immunoassay techniques which include, for example, membrane, solution, or chip based technologies for the detection and/or quantification of nucleic acid or protein.

5           A variety of protocols for detecting and measuring the expression of polynucleotide-encoded products, using either polyclonal or monoclonal antibodies specific for the product are known in the art. Examples include enzyme-linked immunosorbent assay (ELISA), radioimmunoassay (RIA), and fluorescence activated cell sorting (FACS). A two-site, monoclonal-based immunoassay utilizing monoclonal  
10 antibodies reactive to two non-interfering epitopes on a given polypeptide may be preferred for some applications, but a competitive binding assay may also be employed. These and other assays are described, among other places, in Hampton, R. et al. (1990; Serological Methods, a Laboratory Manual, APS Press, St Paul, Minn.) and Maddox, D. E. et al. (1983; *J. Exp. Med.* 158:1211-1216).

15           A wide variety of labels and conjugation techniques are known by those skilled in the art and may be used in various nucleic acid and amino acid assays. Means for producing labeled hybridization or PCR probes for detecting sequences related to polynucleotides include oligolabeling, nick translation, end-labeling or PCR amplification using a labeled nucleotide. Alternatively, the sequences, or any portions  
20 thereof may be cloned into a vector for the production of an mRNA probe. Such vectors are known in the art, are commercially available, and may be used to synthesize RNA probes in vitro by addition of an appropriate RNA polymerase such as T7, T3, or SP6 and labeled nucleotides. These procedures may be conducted using a variety of commercially available kits. Suitable reporter molecules or labels, which may be used  
25 include radionuclides, enzymes, fluorescent, chemiluminescent, or chromogenic agents as well as substrates, cofactors, inhibitors, magnetic particles, and the like.

          Host cells transformed with a polynucleotide sequence of interest may be cultured under conditions suitable for the expression and recovery of the protein from cell culture. The protein produced by a recombinant cell may be secreted or contained  
30 intracellularly depending on the sequence and/or the vector used. As will be understood

by those of skill in the art, expression vectors containing polynucleotides of the invention may be designed to contain signal sequences which direct secretion of the encoded polypeptide through a prokaryotic or eukaryotic cell membrane. Other recombinant constructions may be used to join sequences encoding a polypeptide of interest to nucleotide sequence encoding a polypeptide domain which will facilitate purification of soluble proteins. Such purification facilitating domains include, but are not limited to, metal chelating peptides such as histidine-tryptophan modules that allow purification on immobilized metals, protein A domains that allow purification on immobilized immunoglobulin, and the domain utilized in the FLAGS extension/affinity purification system (Immunex Corp., Seattle, Wash.). The inclusion of cleavable linker sequences such as those specific for Factor XA or enterokinase (Invitrogen, San Diego, Calif.) between the purification domain and the encoded polypeptide may be used to facilitate purification. One such expression vector provides for expression of a fusion protein containing a polypeptide of interest and a nucleic acid encoding 6 histidine residues preceding a thioredoxin or an enterokinase cleavage site. The histidine residues facilitate purification on IMIAC (immobilized metal ion affinity chromatography) as described in Porath, J. et al. (1992, *Prot. Exp. Purif.* 3:263-281) while the enterokinase cleavage site provides a means for purifying the desired polypeptide from the fusion protein. A discussion of vectors which contain fusion proteins is provided in Kroll, D. J. et al. (1993; *DNA Cell Biol.* 12:441-453).

In addition to recombinant production methods, polypeptides of the invention, and fragments thereof, may be produced by direct peptide synthesis using solid-phase techniques (Merrifield J. (1963) *J. Am. Chem. Soc.* 85:2149-2154). Protein synthesis may be performed using manual techniques or by automation. Automated synthesis may be achieved, for example, using Applied Biosystems 431A Peptide Synthesizer (Perkin Elmer). Alternatively, various fragments may be chemically synthesized separately and combined using chemical methods to produce the full length molecule.



Antibody Compositions, Fragments Thereof and Other Binding Agents

According to another aspect, the present invention further provides binding agents, such as antibodies and antigen-binding fragments thereof, that exhibit immunological binding to a tumor polypeptide disclosed herein, or to a portion, variant  
5 or derivative thereof. An antibody, or antigen-binding fragment thereof, is said to "specifically bind," "immunologically bind," and/or is "immunologically reactive" to a polypeptide of the invention if it reacts at a detectable level (within, for example, an ELISA assay) with the polypeptide, and does not react detectably with unrelated polypeptides under similar conditions.

10 Immunological binding, as used in this context, generally refers to the non-covalent interactions of the type which occur between an immunoglobulin molecule and an antigen for which the immunoglobulin is specific. The strength, or affinity of immunological binding interactions can be expressed in terms of the dissociation constant ( $K_d$ ) of the interaction, wherein a smaller  $K_d$  represents a greater  
15 affinity. Immunological binding properties of selected polypeptides can be quantified using methods well known in the art. One such method entails measuring the rates of antigen-binding site/antigen complex formation and dissociation, wherein those rates depend on the concentrations of the complex partners, the affinity of the interaction, and on geometric parameters that equally influence the rate in both directions. Thus, both  
20 the "on rate constant" ( $K_{on}$ ) and the "off rate constant" ( $K_{off}$ ) can be determined by calculation of the concentrations and the actual rates of association and dissociation. The ratio of  $K_{off}/K_{on}$  enables cancellation of all parameters not related to affinity, and is thus equal to the dissociation constant  $K_d$ . See, generally, Davies et al. (1990) Annual Rev. Biochem. 59:439-473.

25 An "antigen-binding site," or "binding portion" of an antibody refers to the part of the immunoglobulin molecule that participates in antigen binding. The antigen binding site is formed by amino acid residues of the N-terminal variable ("V") regions of the heavy ("H") and light ("L") chains. Three highly divergent stretches within the V regions of the heavy and light chains are referred to as "hypervariable  
30 regions" which are interposed between more conserved flanking stretches known as

"framework regions," or "FRs". Thus the term "FR" refers to amino acid sequences which are naturally found between and adjacent to hypervariable regions in immunoglobulins. In an antibody molecule, the three hypervariable regions of a light chain and the three hypervariable regions of a heavy chain are disposed relative to each other in three dimensional space to form an antigen-binding surface. The antigen-binding surface is complementary to the three-dimensional surface of a bound antigen, and the three hypervariable regions of each of the heavy and light chains are referred to as "complementarity-determining regions," or "CDRs."

Binding agents may be further capable of differentiating between patients with and without a cancer, such as prostate cancer, using the representative assays provided herein. For example, antibodies or other binding agents that bind to a tumor protein will preferably generate a signal indicating the presence of a cancer in at least about 20% of patients with the disease, more preferably at least about 30% of patients. Alternatively, or in addition, the antibody will generate a negative signal indicating the absence of the disease in at least about 90% of individuals without the cancer. To determine whether a binding agent satisfies this requirement, biological samples (e.g., blood, sera, sputum, urine and/or tumor biopsies) from patients with and without a cancer (as determined using standard clinical tests) may be assayed as described herein for the presence of polypeptides that bind to the binding agent. Preferably, a statistically significant number of samples with and without the disease will be assayed. Each binding agent should satisfy the above criteria; however, those of ordinary skill in the art will recognize that binding agents may be used in combination to improve sensitivity.

Any agent that satisfies the above requirements may be a binding agent. For example, a binding agent may be a ribosome, with or without a peptide component, an RNA molecule or a polypeptide. In a preferred embodiment, a binding agent is an antibody or an antigen-binding fragment thereof. Antibodies may be prepared by any of a variety of techniques known to those of ordinary skill in the art. See, e.g., Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In general, antibodies can be produced by cell culture techniques, including the generation

of monoclonal antibodies as described herein, or via transfection of antibody genes into suitable bacterial or mammalian cell hosts, in order to allow for the production of recombinant antibodies. In one technique, an immunogen comprising the polypeptide is initially injected into any of a wide variety of mammals (e.g., mice, rats, rabbits, sheep or goats). In this step, the polypeptides of this invention may serve as the immunogen without modification. Alternatively, particularly for relatively short polypeptides, a superior immune response may be elicited if the polypeptide is joined to a carrier protein, such as bovine serum albumin or keyhole limpet hemocyanin. The immunogen is injected into the animal host, preferably according to a predetermined schedule incorporating one or more booster immunizations, and the animals are bled periodically. Polyclonal antibodies specific for the polypeptide may then be purified from such antisera by, for example, affinity chromatography using the polypeptide coupled to a suitable solid support.

Monoclonal antibodies specific for an antigenic polypeptide of interest may be prepared, for example, using the technique of Kohler and Milstein, *Eur. J. Immunol.* 6:511-519, 1976, and improvements thereto. Briefly, these methods involve the preparation of immortal cell lines capable of producing antibodies having the desired specificity (i.e., reactivity with the polypeptide of interest). Such cell lines may be produced, for example, from spleen cells obtained from an animal immunized as described above. The spleen cells are then immortalized by, for example, fusion with a myeloma cell fusion partner, preferably one that is syngeneic with the immunized animal. A variety of fusion techniques may be employed. For example, the spleen cells and myeloma cells may be combined with a nonionic detergent for a few minutes and then plated at low density on a selective medium that supports the growth of hybrid cells, but not myeloma cells. A preferred selection technique uses HAT (hypoxanthine, aminopterin, thymidine) selection. After a sufficient time, usually about 1 to 2 weeks, colonies of hybrids are observed. Single colonies are selected and their culture supernatants tested for binding activity against the polypeptide. Hybridomas having high reactivity and specificity are preferred.

Monoclonal antibodies may be isolated from the supernatants of growing hybridoma colonies. In addition, various techniques may be employed to enhance the yield, such as injection of the hybridoma cell line into the peritoneal cavity of a suitable vertebrate host, such as a mouse. Monoclonal antibodies may then be harvested from the ascites fluid or the blood. Contaminants may be removed from the antibodies by conventional techniques, such as chromatography, gel filtration, precipitation, and extraction. The polypeptides of this invention may be used in the purification process in, for example, an affinity chromatography step.

A number of therapeutically useful molecules are known in the art which comprise antigen-binding sites that are capable of exhibiting immunological binding properties of an antibody molecule. The proteolytic enzyme papain preferentially cleaves IgG molecules to yield several fragments, two of which (the "F(ab)" fragments) each comprise a covalent heterodimer that includes an intact antigen-binding site. The enzyme pepsin is able to cleave IgG molecules to provide several fragments, including the "F(ab)<sub>2</sub>" fragment which comprises both antigen-binding sites. An "Fv" fragment can be produced by preferential proteolytic cleavage of an IgM, and on rare occasions IgG or IgA immunoglobulin molecule. Fv fragments are, however, more commonly derived using recombinant techniques known in the art. The Fv fragment includes a non-covalent V<sub>H</sub>::V<sub>L</sub> heterodimer including an antigen-binding site which retains much of the antigen recognition and binding capabilities of the native antibody molecule. Inbar et al. (1972) Proc. Nat. Acad. Sci. USA 69:2659-2662; Hochman et al. (1976) Biochem 15:2706-2710; and Ehrlich et al. (1980) Biochem 19:4091-4096.

A single chain Fv ("sFv") polypeptide is a covalently linked V<sub>H</sub>::V<sub>L</sub> heterodimer which is expressed from a gene fusion including V<sub>H</sub>- and V<sub>L</sub>-encoding genes linked by a peptide-encoding linker. Huston et al. (1988) Proc. Nat. Acad. Sci. USA 85(16):5879-5883. A number of methods have been described to discern chemical structures for converting the naturally aggregated--but chemically separated--light and heavy polypeptide chains from an antibody V region into an sFv molecule which will fold into a three dimensional structure substantially similar to the structure of an

antigen-binding site. See, *e.g.*, U.S. Pat. Nos. 5,091,513 and 5,132,405, to Huston et al.; and U.S. Pat. No. 4,946,778, to Ladner et al.

Each of the above-described molecules includes a heavy chain and a light chain CDR set, respectively interposed between a heavy chain and a light chain FR set which provide support to the CDRS and define the spatial relationship of the CDRs relative to each other. As used herein, the term "CDR set" refers to the three hypervariable regions of a heavy or light chain V region. Proceeding from the N-terminus of a heavy or light chain, these regions are denoted as "CDR1," "CDR2," and "CDR3" respectively. An antigen-binding site, therefore, includes six CDRs, comprising the CDR set from each of a heavy and a light chain V region. A polypeptide comprising a single CDR, (*e.g.*, a CDR1, CDR2 or CDR3) is referred to herein as a "molecular recognition unit." Crystallographic analysis of a number of antigen-antibody complexes has demonstrated that the amino acid residues of CDRs form extensive contact with bound antigen, wherein the most extensive antigen contact is with the heavy chain CDR3. Thus, the molecular recognition units are primarily responsible for the specificity of an antigen-binding site.

As used herein, the term "FR set" refers to the four flanking amino acid sequences which frame the CDRs of a CDR set of a heavy or light chain V region. Some FR residues may contact bound antigen; however, FRs are primarily responsible for folding the V region into the antigen-binding site, particularly the FR residues directly adjacent to the CDRS. Within FRs, certain amino residues and certain structural features are very highly conserved. In this regard, all V region sequences contain an internal disulfide loop of around 90 amino acid residues. When the V regions fold into a binding-site, the CDRs are displayed as projecting loop motifs which form an antigen-binding surface. It is generally recognized that there are conserved structural regions of FRs which influence the folded shape of the CDR loops into certain "canonical" structures--regardless of the precise CDR amino acid sequence. Further, certain FR residues are known to participate in non-covalent interdomain contacts which stabilize the interaction of the antibody heavy and light chains.

A number of "humanized" antibody molecules comprising an antigen-binding site derived from a non-human immunoglobulin have been described, including chimeric antibodies having rodent V regions and their associated CDRs fused to human constant domains (Winter et al. (1991) *Nature* 349:293-299; Lobuglio et al. (1989) *Proc. Nat. Acad. Sci. USA* 86:4220-4224; Shaw et al. (1987) *J Immunol.* 138:4534-4538; and Brown et al. (1987) *Cancer Res.* 47:3577-3583), rodent CDRs grafted into a human supporting FR prior to fusion with an appropriate human antibody constant domain (Riechmann et al. (1988) *Nature* 332:323-327; Verhoeyen et al. (1988) *Science* 239:1534-1536; and Jones et al. (1986) *Nature* 321:522-525), and rodent CDRs supported by recombinantly veneered rodent FRs (European Patent Publication No. 519,596, published Dec. 23, 1992). These "humanized" molecules are designed to minimize unwanted immunological response toward rodent antihuman antibody molecules which limits the duration and effectiveness of therapeutic applications of those moieties in human recipients.

As used herein, the terms "veneered FRs" and "recombinantly veneered FRs" refer to the selective replacement of FR residues from, *e.g.*, a rodent heavy or light chain V region, with human FR residues in order to provide a xenogeneic molecule comprising an antigen-binding site which retains substantially all of the native FR polypeptide folding structure. Veneering techniques are based on the understanding that the ligand binding characteristics of an antigen-binding site are determined primarily by the structure and relative disposition of the heavy and light chain CDR sets within the antigen-binding surface. Davies et al. (1990) *Ann. Rev. Biochem.* 59:439-473. Thus, antigen binding specificity can be preserved in a humanized antibody only wherein the CDR structures, their interaction with each other, and their interaction with the rest of the V region domains are carefully maintained. By using veneering techniques, exterior (*e.g.*, solvent-accessible) FR residues which are readily encountered by the immune system are selectively replaced with human residues to provide a hybrid molecule that comprises either a weakly immunogenic, or substantially non-immunogenic veneered surface.

The process of veneering makes use of the available sequence data for human antibody variable domains compiled by Kabat et al., in Sequences of Proteins of Immunological Interest, 4th ed., (U.S. Dept. of Health and Human Services, U.S. Government Printing Office, 1987), updates to the Kabat database, and other accessible  
5 U.S. and foreign databases (both nucleic acid and protein). Solvent accessibilities of V region amino acids can be deduced from the known three-dimensional structure for human and murine antibody fragments. There are two general steps in veneering a murine antigen-binding site. Initially, the FRs of the variable domains of an antibody molecule of interest are compared with corresponding FR sequences of human variable  
10 domains obtained from the above-identified sources. The most homologous human V regions are then compared residue by residue to corresponding murine amino acids. The residues in the murine FR which differ from the human counterpart are replaced by the residues present in the human moiety using recombinant techniques well known in the art. Residue switching is only carried out with moieties which are at least partially  
15 exposed (solvent accessible), and care is exercised in the replacement of amino acid residues which may have a significant effect on the tertiary structure of V region domains, such as proline, glycine and charged amino acids.

In this manner, the resultant "veneered" murine antigen-binding sites are thus designed to retain the murine CDR residues, the residues substantially adjacent to  
20 the CDRs, the residues identified as buried or mostly buried (solvent inaccessible), the residues believed to participate in non-covalent (*e.g.*, electrostatic and hydrophobic) contacts between heavy and light chain domains, and the residues from conserved structural regions of the FRs which are believed to influence the "canonical" tertiary structures of the CDR loops. These design criteria are then used to prepare recombinant  
25 nucleotide sequences which combine the CDRs of both the heavy and light chain of a murine antigen-binding site into human-appearing FRs that can be used to transfect mammalian cells for the expression of recombinant human antibodies which exhibit the antigen specificity of the murine antibody molecule.

In another embodiment of the invention, monoclonal antibodies of the  
30 present invention may be coupled to one or more therapeutic agents. Suitable agents in

this regard include radionuclides, differentiation inducers, drugs, toxins, and derivatives thereof. Preferred radionuclides include  $^{90}\text{Y}$ ,  $^{123}\text{I}$ ,  $^{125}\text{I}$ ,  $^{131}\text{I}$ ,  $^{186}\text{Re}$ ,  $^{188}\text{Re}$ ,  $^{211}\text{At}$ , and  $^{212}\text{Bi}$ . Preferred drugs include methotrexate, and pyrimidine and purine analogs. Preferred differentiation inducers include phorbol esters and butyric acid. Preferred  
5 toxins include ricin, abrin, diphtheria toxin, cholera toxin, gelonin, *Pseudomonas* exotoxin, Shigella toxin, and pokeweed antiviral protein.

A therapeutic agent may be coupled (*e.g.*, covalently bonded) to a suitable monoclonal antibody either directly or indirectly (*e.g.*, via a linker group). A direct reaction between an agent and an antibody is possible when each possesses a  
10 substituent capable of reacting with the other. For example, a nucleophilic group, such as an amino or sulfhydryl group, on one may be capable of reacting with a carbonyl-containing group, such as an anhydride or an acid halide, or with an alkyl group containing a good leaving group (*e.g.*, a halide) on the other.

Alternatively, it may be desirable to couple a therapeutic agent and an  
15 antibody via a linker group. A linker group can function as a spacer to distance an antibody from an agent in order to avoid interference with binding capabilities. A linker group can also serve to increase the chemical reactivity of a substituent on an agent or an antibody, and thus increase the coupling efficiency. An increase in chemical reactivity may also facilitate the use of agents, or functional groups on agents, which  
20 otherwise would not be possible.

It will be evident to those skilled in the art that a variety of bifunctional or polyfunctional reagents, both homo- and hetero-functional (such as those described in the catalog of the Pierce Chemical Co., Rockford, IL), may be employed as the linker group. Coupling may be effected, for example, through amino groups, carboxyl groups,  
25 sulfhydryl groups or oxidized carbohydrate residues. There are numerous references describing such methodology, *e.g.*, U.S. Patent No. 4,671,958, to Rodwell et al.

Where a therapeutic agent is more potent when free from the antibody portion of the immunoconjugates of the present invention, it may be desirable to use a linker group which is cleavable during or upon internalization into a cell. A number of  
30 different cleavable linker groups have been described. The mechanisms for the



intracellular release of an agent from these linker groups include cleavage by reduction of a disulfide bond (*e.g.*, U.S. Patent No. 4,489,710, to Spitler), by irradiation of a photolabile bond (*e.g.*, U.S. Patent No. 4,625,014, to Senter et al.), by hydrolysis of derivatized amino acid side chains (*e.g.*, U.S. Patent No. 4,638,045, to Kohn et al.), by  
5 serum complement-mediated hydrolysis (*e.g.*, U.S. Patent No. 4,671,958, to Rodwell et al.), and acid-catalyzed hydrolysis (*e.g.*, U.S. Patent No. 4,569,789, to Blattler et al.).

It may be desirable to couple more than one agent to an antibody. In one embodiment, multiple molecules of an agent are coupled to one antibody molecule. In another embodiment, more than one type of agent may be coupled to one antibody.  
10 Regardless of the particular embodiment, immunoconjugates with more than one agent may be prepared in a variety of ways. For example, more than one agent may be coupled directly to an antibody molecule, or linkers that provide multiple sites for attachment can be used. Alternatively, a carrier can be used.

A carrier may bear the agents in a variety of ways, including covalent  
15 bonding either directly or via a linker group. Suitable carriers include proteins such as albumins (*e.g.*, U.S. Patent No. 4,507,234, to Kato et al.), peptides and polysaccharides such as aminodextran (*e.g.*, U.S. Patent No. 4,699,784, to Shih et al.). A carrier may also bear an agent by noncovalent bonding or by encapsulation, such as within a liposome vesicle (*e.g.*, U.S. Patent Nos. 4,429,008 and 4,873,088). Carriers specific for  
20 radionuclide agents include radiohalogenated small molecules and chelating compounds. For example, U.S. Patent No. 4,735,792 discloses representative radiohalogenated small molecules and their synthesis. A radionuclide chelate may be formed from chelating compounds that include those containing nitrogen and sulfur atoms as the donor atoms for binding the metal, or metal oxide, radionuclide. For  
25 example, U.S. Patent No. 4,673,562, to Davison et al. discloses representative chelating compounds and their synthesis.

#### T Cell Compositions

The present invention, in another aspect, provides T cells specific for a tumor polypeptide disclosed herein, or for a variant or derivative thereof. Such cells

may generally be prepared *in vitro* or *ex vivo*, using standard procedures. For example, T cells may be isolated from bone marrow, peripheral blood, or a fraction of bone marrow or peripheral blood of a patient, using a commercially available cell separation system, such as the Isolex™ System, available from Nexell Therapeutics, Inc. (Irvine, CA; see also U.S. Patent No. 5,240,856; U.S. Patent No. 5,215,926; WO 89/06280; WO 91/16116 and WO 92/07243). Alternatively, T cells may be derived from related or unrelated humans, non-human mammals, cell lines or cultures.

T cells may be stimulated with a polypeptide, polynucleotide encoding a polypeptide and/or an antigen presenting cell (APC) that expresses such a polypeptide. Such stimulation is performed under conditions and for a time sufficient to permit the generation of T cells that are specific for the polypeptide of interest. Preferably, a tumor polypeptide or polynucleotide of the invention is present within a delivery vehicle, such as a microsphere, to facilitate the generation of specific T cells.

T cells are considered to be specific for a polypeptide of the present invention if the T cells specifically proliferate, secrete cytokines or kill target cells coated with the polypeptide or expressing a gene encoding the polypeptide. T cell specificity may be evaluated using any of a variety of standard techniques. For example, within a chromium release assay or proliferation assay, a stimulation index of more than two fold increase in lysis and/or proliferation, compared to negative controls, indicates T cell specificity. Such assays may be performed, for example, as described in Chen et al., *Cancer Res.* 54:1065-1070, 1994. Alternatively, detection of the proliferation of T cells may be accomplished by a variety of known techniques. For example, T cell proliferation can be detected by measuring an increased rate of DNA synthesis (*e.g.*, by pulse-labeling cultures of T cells with tritiated thymidine and measuring the amount of tritiated thymidine incorporated into DNA). Contact with a tumor polypeptide (100 ng/ml - 100 µg/ml, preferably 200 ng/ml - 25 µg/ml) for 3 - 7 days will typically result in at least a two fold increase in proliferation of the T cells. Contact as described above for 2-3 hours should result in activation of the T cells, as measured using standard cytokine assays in which a two fold increase in the level of cytokine release (*e.g.*, TNF or IFN-γ) is indicative of T cell activation (*see* Coligan et

al., Current Protocols in Immunology, vol. 1, Wiley Interscience (Greene 1998)). T cells that have been activated in response to a tumor polypeptide, polynucleotide or polypeptide-expressing APC may be CD4<sup>+</sup> and/or CD8<sup>+</sup>. Tumor polypeptide-specific T cells may be expanded using standard techniques. Within preferred embodiments, the T cells are derived from a patient, a related donor or an unrelated donor, and are administered to the patient following stimulation and expansion.

For therapeutic purposes, CD4<sup>+</sup> or CD8<sup>+</sup> T cells that proliferate in response to a tumor polypeptide, polynucleotide or APC can be expanded in number either *in vitro* or *in vivo*. Proliferation of such T cells *in vitro* may be accomplished in a variety of ways. For example, the T cells can be re-exposed to a tumor polypeptide, or a short peptide corresponding to an immunogenic portion of such a polypeptide, with or without the addition of T cell growth factors, such as interleukin-2, and/or stimulator cells that synthesize a tumor polypeptide. Alternatively, one or more T cells that proliferate in the presence of the tumor polypeptide can be expanded in number by cloning. Methods for cloning cells are well known in the art, and include limiting dilution.

#### Pharmaceutical Compositions

In additional embodiments, the present invention concerns formulation of one or more of the polynucleotide, polypeptide, T-cell and/or antibody compositions disclosed herein in pharmaceutically-acceptable carriers for administration to a cell or an animal, either alone, or in combination with one or more other modalities of therapy.

It will be understood that, if desired, a composition as disclosed herein may be administered in combination with other agents as well, such as, *e.g.*, other proteins or polypeptides or various pharmaceutically-active agents. In fact, there is virtually no limit to other components that may also be included, given that the additional agents do not cause a significant adverse effect upon contact with the target cells or host tissues. The compositions may thus be delivered along with various other agents as required in the particular instance. Such compositions may be purified from host cells or other biological sources, or alternatively may be chemically synthesized as

described herein. Likewise, such compositions may further comprise substituted or derivatized RNA or DNA compositions.

Therefore, in another aspect of the present invention, pharmaceutical compositions are provided comprising one or more of the polynucleotide, polypeptide, antibody, and/or T-cell compositions described herein in combination with a physiologically acceptable carrier. In certain preferred embodiments, the pharmaceutical compositions of the invention comprise immunogenic polynucleotide and/or polypeptide compositions of the invention for use in prophylactic and therapeutic vaccine applications. Vaccine preparation is generally described in, for example, M.F. Powell and M.J. Newman, eds., "Vaccine Design (the subunit and adjuvant approach)," Plenum Press (NY, 1995). Generally, such compositions will comprise one or more polynucleotide and/or polypeptide compositions of the present invention in combination with one or more immunostimulants.

It will be apparent that any of the pharmaceutical compositions described herein can contain pharmaceutically acceptable salts of the polynucleotides and polypeptides of the invention. Such salts can be prepared, for example, from pharmaceutically acceptable non-toxic bases, including organic bases (e.g., salts of primary, secondary and tertiary amines and basic amino acids) and inorganic bases (e.g., sodium, potassium, lithium, ammonium, calcium and magnesium salts).

In another embodiment, illustrative immunogenic compositions, e.g., vaccine compositions, of the present invention comprise DNA encoding one or more of the polypeptides as described above, such that the polypeptide is generated *in situ*. As noted above, the polynucleotide may be administered within any of a variety of delivery systems known to those of ordinary skill in the art. Indeed, numerous gene delivery techniques are well known in the art, such as those described by Rolland, *Crit. Rev. Therap. Drug Carrier Systems* 15:143-198, 1998, and references cited therein. Appropriate polynucleotide expression systems will, of course, contain the necessary regulatory DNA regulatory sequences for expression in a patient (such as a suitable promoter and terminating signal). Alternatively, bacterial delivery systems may involve

the administration of a bacterium (such as *Bacillus-Calmette-Guerrin*) that expresses an immunogenic portion of the polypeptide on its cell surface or secretes such an epitope.

Therefore, in certain embodiments, polynucleotides encoding immunogenic polypeptides described herein are introduced into suitable mammalian host cells for expression using any of a number of known viral-based systems. In one illustrative embodiment, retroviruses provide a convenient and effective platform for gene delivery systems. A selected nucleotide sequence encoding a polypeptide of the present invention can be inserted into a vector and packaged in retroviral particles using techniques known in the art. The recombinant virus can then be isolated and delivered to a subject. A number of illustrative retroviral systems have been described (*e.g.*, U.S. Pat. No. 5,219,740; Miller and Rosman (1989) *BioTechniques* 7:980-990; Miller, A. D. (1990) *Human Gene Therapy* 1:5-14; Scarpa et al. (1991) *Virology* 180:849-852; Burns et al. (1993) *Proc. Natl. Acad. Sci. USA* 90:8033-8037; and Boris-Lawrie and Temin (1993) *Cur. Opin. Genet. Develop.* 3:102-109.

In addition, a number of illustrative adenovirus-based systems have also been described. Unlike retroviruses which integrate into the host genome, adenoviruses persist extrachromosomally thus minimizing the risks associated with insertional mutagenesis (Haj-Ahmad and Graham (1986) *J. Virol.* 57:267-274; Bett et al. (1993) *J. Virol.* 67:5911-5921; Mittereder et al. (1994) *Human Gene Therapy* 5:717-729; Seth et al. (1994) *J. Virol.* 68:933-940; Barr et al. (1994) *Gene Therapy* 1:51-58; Berkner, K. L. (1988) *BioTechniques* 6:616-629; and Rich et al. (1993) *Human Gene Therapy* 4:461-476).

Various adeno-associated virus (AAV) vector systems have also been developed for polynucleotide delivery. AAV vectors can be readily constructed using techniques well known in the art. See, *e.g.*, U.S. Pat. Nos. 5,173,414 and 5,139,941; International Publication Nos. WO 92/01070 and WO 93/03769; Lebkowski et al. (1988) *Molec. Cell. Biol.* 8:3988-3996; Vincent et al. (1990) *Vaccines 90* (Cold Spring Harbor Laboratory Press); Carter, B. J. (1992) *Current Opinion in Biotechnology* 3:533-539; Muzyczka, N. (1992) *Current Topics in Microbiol. and Immunol.* 158:97-129;

Kotin, R. M. (1994) Human Gene Therapy 5:793-801; Shelling and Smith (1994) Gene Therapy 1:165-169; and Zhou et al. (1994) J. Exp. Med. 179:1867-1875.

Additional viral vectors useful for delivering the polynucleotides encoding polypeptides of the present invention by gene transfer include those derived from the pox family of viruses, such as vaccinia virus and avian poxvirus. By way of example, vaccinia virus recombinants expressing the novel molecules can be constructed as follows. The DNA encoding a polypeptide is first inserted into an appropriate vector so that it is adjacent to a vaccinia promoter and flanking vaccinia DNA sequences, such as the sequence encoding thymidine kinase (TK). This vector is then used to transfect cells which are simultaneously infected with vaccinia. Homologous recombination serves to insert the vaccinia promoter plus the gene encoding the polypeptide of interest into the viral genome. The resulting TK.sup.(-) recombinant can be selected by culturing the cells in the presence of 5-bromodeoxyuridine and picking viral plaques resistant thereto.

A vaccinia-based infection/transfection system can be conveniently used to provide for inducible, transient expression or coexpression of one or more polypeptides described herein in host cells of an organism. In this particular system, cells are first infected in vitro with a vaccinia virus recombinant that encodes the bacteriophage T7 RNA polymerase. This polymerase displays exquisite specificity in that it only transcribes templates bearing T7 promoters. Following infection, cells are transfected with the polynucleotide or polynucleotides of interest, driven by a T7 promoter. The polymerase expressed in the cytoplasm from the vaccinia virus recombinant transcribes the transfected DNA into RNA which is then translated into polypeptide by the host translational machinery. The method provides for high level, transient, cytoplasmic production of large quantities of RNA and its translation products. See, *e.g.*, Elroy-Stein and Moss, Proc. Natl. Acad. Sci. USA (1990) 87:6743-6747; Fuerst et al. Proc. Natl. Acad. Sci. USA (1986) 83:8122-8126.

Alternatively, avipoxviruses, such as the fowlpox and canarypox viruses, can also be used to deliver the coding sequences of interest. Recombinant avipox viruses, expressing immunogens from mammalian pathogens, are known to confer

protective immunity when administered to non-avian species. The use of an Avipox vector is particularly desirable in human and other mammalian species since members of the Avipox genus can only productively replicate in susceptible avian species and therefore are not infective in mammalian cells. Methods for producing recombinant  
5 Avipoxviruses are known in the art and employ genetic recombination, as described above with respect to the production of vaccinia viruses. See, e.g., WO 91/12882; WO 89/03429; and WO 92/03545.

Any of a number of alphavirus vectors can also be used for delivery of polynucleotide compositions of the present invention, such as those vectors described in  
10 U.S. Patent Nos. 5,843,723; 6,015,686; 6,008,035 and 6,015,694. Certain vectors based on Venezuelan Equine Encephalitis (VEE) can also be used, illustrative examples of which can be found in U.S. Patent Nos. 5,505,947 and 5,643,576.

Moreover, molecular conjugate vectors, such as the adenovirus chimeric vectors described in Michael et al. *J. Biol. Chem.* (1993) 268:6866-6869 and Wagner et  
15 al. *Proc. Natl. Acad. Sci. USA* (1992) 89:6099-6103, can also be used for gene delivery under the invention.

Additional illustrative information on these and other known viral-based delivery systems can be found, for example, in Fisher-Hoch et al., *Proc. Natl. Acad. Sci. USA* 86:317-321, 1989; Flexner et al., *Ann. N.Y. Acad. Sci.* 569:86-103, 1989; Flexner  
20 et al., *Vaccine* 8:17-21, 1990; U.S. Patent Nos. 4,603,112, 4,769,330, and 5,017,487; WO 89/01973; U.S. Patent No. 4,777,127; GB 2,200,651; EP 0,345,242; WO 91/02805; Berkner, *Biotechniques* 6:616-627, 1988; Rosenfeld et al., *Science* 252:431-434, 1991; Kolls et al., *Proc. Natl. Acad. Sci. USA* 91:215-219, 1994; Kass-Eisler et al., *Proc. Natl. Acad. Sci. USA* 90:11498-11502, 1993; Guzman et al.,  
25 *Circulation* 88:2838-2848, 1993; and Guzman et al., *Cir. Res.* 73:1202-1207, 1993.

In certain embodiments, a polynucleotide may be integrated into the genome of a target cell. This integration may be in a specific location and orientation via homologous recombination (gene replacement) or it may be integrated in a random, non-specific location (gene augmentation). In yet further embodiments, the  
30 polynucleotide may be stably maintained in the cell as a separate, episomal segment of

DNA. Such polynucleotide segments or "episomes" encode sequences sufficient to permit maintenance and replication independent of or in synchronization with the host cell cycle. The manner in which the expression construct is delivered to a cell and where in the cell the polynucleotide remains is dependent on the type of expression  
5 construct employed.

In another embodiment of the invention, a polynucleotide is administered/delivered as "naked" DNA, for example as described in Ulmer et al., *Science* 259:1745-1749, 1993 and reviewed by Cohen, *Science* 259:1691-1692, 1993. The uptake of naked DNA may be increased by coating the DNA onto biodegradable  
10 beads, which are efficiently transported into the cells.

In still another embodiment, a composition of the present invention can be delivered via a particle bombardment approach, many of which have been described. In one illustrative example, gas-driven particle acceleration can be achieved with devices such as those manufactured by Powderject Pharmaceuticals PLC (Oxford, UK)  
15 and Powderject Vaccines Inc. (Madison, WI), some examples of which are described in U.S. Patent Nos. 5,846,796; 6,010,478; 5,865,796; 5,584,807; and EP Patent No. 0500 799. This approach offers a needle-free delivery approach wherein a dry powder formulation of microscopic particles, such as polynucleotide or polypeptide particles, are accelerated to high speed within a helium gas jet generated by a hand held device,  
20 propelling the particles into a target tissue of interest.

In a related embodiment, other devices and methods that may be useful for gas-driven needle-less injection of compositions of the present invention include those provided by Bioject, Inc. (Portland, OR), some examples of which are described in U.S. Patent Nos. 4,790,824; 5,064,413; 5,312,335; 5,383,851; 5,399,163; 5,520,639  
25 and 5,993,412.

According to another embodiment, the pharmaceutical compositions described herein will comprise one or more immunostimulants in addition to the immunogenic polynucleotide, polypeptide, antibody, T-cell and/or APC compositions of this invention. An immunostimulant refers to essentially any substance that enhances  
30 or potentiates an immune response (antibody and/or cell-mediated) to an exogenous



antigen. One preferred type of immunostimulant comprises an adjuvant. Many adjuvants contain a substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil, and a stimulator of immune responses, such as lipid A, *Bordetella pertussis* or *Mycobacterium tuberculosis* derived proteins.

5 Certain adjuvants are commercially available as, for example, Freund's Incomplete Adjuvant and Complete Adjuvant (Difco Laboratories, Detroit, MI); Merck Adjuvant 65 (Merck and Company, Inc., Rahway, NJ); AS-2 (SmithKline Beecham, Philadelphia, PA); aluminum salts such as aluminum hydroxide gel (alum) or aluminum phosphate; salts of calcium, iron or zinc; an insoluble suspension of acylated tyrosine; acylated

10 sugars; cationically or anionically derivatized polysaccharides; polyphosphazenes; biodegradable microspheres; monophosphoryl lipid A and quil A. Cytokines, such as GM-CSF, interleukin-2, -7, -12, and other like growth factors, may also be used as adjuvants.

Within certain embodiments of the invention, the adjuvant composition

15 is preferably one that induces an immune response predominantly of the Th1 type. High levels of Th1-type cytokines (*e.g.*, IFN- $\gamma$ , TNF $\alpha$ , IL-2 and IL-12) tend to favor the induction of cell mediated immune responses to an administered antigen. In contrast, high levels of Th2-type cytokines (*e.g.*, IL-4, IL-5, IL-6 and IL-10) tend to favor the induction of humoral immune responses. Following application of a vaccine as

20 provided herein, a patient will support an immune response that includes Th1- and Th2-type responses. Within a preferred embodiment, in which a response is predominantly Th1-type, the level of Th1-type cytokines will increase to a greater extent than the level of Th2-type cytokines. The levels of these cytokines may be readily assessed using standard assays. For a review of the families of cytokines, see Mosmann and Coffman,

25 *Ann. Rev. Immunol.* 7:145-173, 1989.

Certain preferred adjuvants for eliciting a predominantly Th1-type response include, for example, a combination of monophosphoryl lipid A, preferably 3-de-O-acylated monophosphoryl lipid A, together with an aluminum salt. MPL<sup>®</sup> adjuvants are available from Corixa Corporation (Seattle, WA; *see*, for example, US

30 Patent Nos. 4,436,727; 4,877,611; 4,866,034 and 4,912,094). CpG-containing

oligonucleotides (in which the CpG dinucleotide is unmethylated) also induce a predominantly Th1 response. Such oligonucleotides are well known and are described, for example, in WO 96/02555, WO 99/33488 and U.S. Patent Nos. 6,008,200 and 5,856,462. Immunostimulatory DNA sequences are also described, for example, by

5 Sato et al., *Science* 273:352, 1996. Another preferred adjuvant comprises a saponin, such as Quil A, or derivatives thereof, including QS21 and QS7 (Aquila Biopharmaceuticals Inc., Framingham, MA); Escin; Digitonin; or *Gypsophila* or *Chenopodium quinoa* saponins. Other preferred formulations include more than one saponin in the adjuvant combinations of the present invention, for example

10 combinations of at least two of the following group comprising QS21, QS7, Quil A,  $\beta$ -escin, or digitonin.

Alternatively the saponin formulations may be combined with vaccine vehicles composed of chitosan or other polycationic polymers, polylactide and polylactide-co-glycolide particles, poly-N-acetyl glucosamine-based polymer matrix,

15 particles composed of polysaccharides or chemically modified polysaccharides, liposomes and lipid-based particles, particles composed of glycerol monoesters, etc. The saponins may also be formulated in the presence of cholesterol to form particulate structures such as liposomes or ISCOMs. Furthermore, the saponins may be formulated together with a polyoxyethylene ether or ester, in either a non-particulate solution or

20 suspension, or in a particulate structure such as a paucilamellar liposome or ISCOM. The saponins may also be formulated with excipients such as Carbopol<sup>R</sup> to increase viscosity, or may be formulated in a dry powder form with a powder excipient such as lactose.

In one preferred embodiment, the adjuvant system includes the

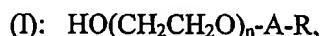
25 combination of a monophosphoryl lipid A and a saponin derivative, such as the combination of QS21 and 3D-MPL<sup>®</sup> adjuvant, as described in WO 94/00153, or a less reactogenic composition where the QS21 is quenched with cholesterol, as described in WO 96/33739. Other preferred formulations comprise an oil-in-water emulsion and tocopherol. Another particularly preferred adjuvant formulation employing QS21, 3D-

MPL<sup>®</sup> adjuvant and tocopherol in an oil-in-water emulsion is described in WO 95/17210.

Another enhanced adjuvant system involves the combination of a CpG-containing oligonucleotide and a saponin derivative particularly the combination of CpG and QS21 is disclosed in WO 00/09159. Preferably the formulation additionally comprises an oil in water emulsion and tocopherol.

Additional illustrative adjuvants for use in the pharmaceutical compositions of the invention include Montanide ISA 720 (Seppic, France), SAF (Chiron, California, United States), ISCOMS (CSL), MF-59 (Chiron), the SBAS series of adjuvants (*e.g.*, SBAS-2 or SBAS-4, available from SmithKline Beecham, Rixensart, Belgium), Detox (Enhanzyn<sup>®</sup>; Corixa, Hamilton, MT), RC-529 (Corixa, Hamilton, MT) and other aminoalkyl glucosaminide 4-phosphates (AGPs), such as those described in pending U.S. Patent Application Serial Nos. 08/853,826 and 09/074,720, the disclosures of which are incorporated herein by reference in their entireties, and polyoxyethylene ether adjuvants such as those described in WO 99/52549A1.

Other preferred adjuvants include adjuvant molecules of the general formula



wherein, *n* is 1-50, A is a bond or -C(O)-, R is C<sub>1-50</sub> alkyl or Phenyl C<sub>1-50</sub> alkyl.

One embodiment of the present invention consists of a vaccine formulation comprising a polyoxyethylene ether of general formula (I), wherein *n* is between 1 and 50, preferably 4-24, most preferably 9; the R component is C<sub>1-50</sub>, preferably C<sub>4</sub>-C<sub>20</sub> alkyl and most preferably C<sub>12</sub> alkyl, and A is a bond. The concentration of the polyoxyethylene ethers should be in the range 0.1-20%, preferably from 0.1-10%, and most preferably in the range 0.1-1%. Preferred polyoxyethylene ethers are selected from the following group: polyoxyethylene-9-lauryl ether, polyoxyethylene-9-stearyl ether, polyoxyethylene-8-stearyl ether, polyoxyethylene-4-lauryl ether, polyoxyethylene-35-lauryl ether, and polyoxyethylene-23-lauryl ether. Polyoxyethylene ethers such as polyoxyethylene lauryl ether are described in the Merck index (12<sup>th</sup> edition: entry 7717). These adjuvant molecules are described in WO

99/52549. The polyoxyethylene ether according to the general formula (I) above may, if desired, be combined with another adjuvant. For example, a preferred adjuvant combination is preferably with CpG as described in the pending UK patent application GB 9820956.2.

5           According to another embodiment of this invention, an immunogenic composition described herein is delivered to a host via antigen presenting cells (APCs), such as dendritic cells, macrophages, B cells, monocytes and other cells that may be engineered to be efficient APCs. Such cells may, but need not, be genetically modified to increase the capacity for presenting the antigen, to improve activation and/or  
10 maintenance of the T cell response, to have anti-tumor effects *per se* and/or to be immunologically compatible with the receiver (*i.e.*, matched HLA haplotype). APCs may generally be isolated from any of a variety of biological fluids and organs, including tumor and peritumoral tissues, and may be autologous, allogeneic, syngeneic or xenogeneic cells.

15           Certain preferred embodiments of the present invention use dendritic cells or progenitors thereof as antigen-presenting cells. Dendritic cells are highly potent APCs (Banchereau and Steinman, *Nature* 392:245-251, 1998) and have been shown to be effective as a physiological adjuvant for eliciting prophylactic or therapeutic antitumor immunity (*see* Timmerman and Levy, *Ann. Rev. Med.* 50:507-529, 1999). In  
20 general, dendritic cells may be identified based on their typical shape (stellate *in situ*, with marked cytoplasmic processes (dendrites) visible *in vitro*), their ability to take up, process and present antigens with high efficiency and their ability to activate naïve T cell responses. Dendritic cells may, of course, be engineered to express specific cell-surface receptors or ligands that are not commonly found on dendritic cells *in vivo* or *ex*  
25 *vivo*, and such modified dendritic cells are contemplated by the present invention. As an alternative to dendritic cells, secreted vesicles antigen-loaded dendritic cells (called exosomes) may be used within a vaccine (*see* Zitvogel et al., *Nature Med.* 4:594-600, 1998).

          Dendritic cells and progenitors may be obtained from peripheral blood,  
30 bone marrow, tumor-infiltrating cells, peritumoral tissues-infiltrating cells, lymph

nodes, spleen, skin, umbilical cord blood or any other suitable tissue or fluid. For example, dendritic cells may be differentiated *ex vivo* by adding a combination of cytokines such as GM-CSF, IL-4, IL-13 and/or TNF $\alpha$  to cultures of monocytes harvested from peripheral blood. Alternatively, CD34 positive cells harvested from  
5 peripheral blood, umbilical cord blood or bone marrow may be differentiated into dendritic cells by adding to the culture medium combinations of GM-CSF, IL-3, TNF $\alpha$ , CD40 ligand, LPS, flt3 ligand and/or other compound(s) that induce differentiation, maturation and proliferation of dendritic cells.

Dendritic cells are conveniently categorized as "immature" and "mature"  
10 cells, which allows a simple way to discriminate between two well characterized phenotypes. However, this nomenclature should not be construed to exclude all possible intermediate stages of differentiation. Immature dendritic cells are characterized as APC with a high capacity for antigen uptake and processing, which correlates with the high expression of Fc $\gamma$  receptor and mannose receptor. The mature  
15 phenotype is typically characterized by a lower expression of these markers, but a high expression of cell surface molecules responsible for T cell activation such as class I and class II MHC, adhesion molecules (*e.g.*, CD54 and CD11) and costimulatory molecules (*e.g.*, CD40, CD80, CD86 and 4-1BB).

APCs may generally be transfected with a polynucleotide of the  
20 invention (or portion or other variant thereof) such that the encoded polypeptide, or an immunogenic portion thereof, is expressed on the cell surface. Such transfection may take place *ex vivo*, and a pharmaceutical composition comprising such transfected cells may then be used for therapeutic purposes, as described herein. Alternatively, a gene delivery vehicle that targets a dendritic or other antigen presenting cell may be  
25 administered to a patient, resulting in transfection that occurs *in vivo*. *In vivo* and *ex vivo* transfection of dendritic cells, for example, may generally be performed using any methods known in the art, such as those described in WO 97/24447, or the gene gun approach described by Mahvi et al., *Immunology and cell Biology* 75:456-460, 1997. Antigen loading of dendritic cells may be achieved by incubating dendritic cells or  
30 progenitor cells with the tumor polypeptide, DNA (naked or within a plasmid vector) or

RNA; or with antigen-expressing recombinant bacterium or viruses (*e.g.*, vaccinia, fowlpox, adenovirus or lentivirus vectors). Prior to loading, the polypeptide may be covalently conjugated to an immunological partner that provides T cell help (*e.g.*, a carrier molecule). Alternatively, a dendritic cell may be pulsed with a non-conjugated  
5 immunological partner, separately or in the presence of the polypeptide.

While any suitable carrier known to those of ordinary skill in the art may be employed in the pharmaceutical compositions of this invention, the type of carrier will typically vary depending on the mode of administration. Compositions of the present invention may be formulated for any appropriate manner of administration,  
10 including for example, topical, oral, nasal, mucosal, intravenous, intracranial, intraperitoneal, subcutaneous and intramuscular administration.

Carriers for use within such pharmaceutical compositions are biocompatible, and may also be biodegradable. In certain embodiments, the formulation preferably provides a relatively constant level of active component release.  
15 In other embodiments, however, a more rapid rate of release immediately upon administration may be desired. The formulation of such compositions is well within the level of ordinary skill in the art using known techniques. Illustrative carriers useful in this regard include microparticles of poly(lactide-co-glycolide), polyacrylate, latex, starch, cellulose, dextran and the like. Other illustrative delayed-release carriers  
20 include supramolecular biovectors, which comprise a non-liquid hydrophilic core (*e.g.*, a cross-linked polysaccharide or oligosaccharide) and, optionally, an external layer comprising an amphiphilic compound, such as a phospholipid (*see e.g.*, U.S. Patent No. 5,151,254 and PCT applications WO 94/20078, WO/94/23701 and WO 96/06638). The amount of active compound contained within a sustained release formulation depends  
25 upon the site of implantation, the rate and expected duration of release and the nature of the condition to be treated or prevented.

In another illustrative embodiment, biodegradable microspheres (*e.g.*, polylactate polyglycolate) are employed as carriers for the compositions of this invention. Suitable biodegradable microspheres are disclosed, for example, in U.S.  
30 Patent Nos. 4,897,268; 5,075,109; 5,928,647; 5,811,128; 5,820,883; 5,853,763;

5,814,344, 5,407,609 and 5,942,252. Modified hepatitis B core protein carrier systems, such as described in WO/99 40934, and references cited therein, will also be useful for many applications. Another illustrative carrier/delivery system employs a carrier comprising particulate-protein complexes, such as those described in U.S. Patent No. 5,928,647, which are capable of inducing a class I-restricted cytotoxic T lymphocyte responses in a host.

The pharmaceutical compositions of the invention will often further comprise one or more buffers (*e.g.*, neutral buffered saline or phosphate buffered saline), carbohydrates (*e.g.*, glucose, mannose, sucrose or dextrans), mannitol, proteins, polypeptides or amino acids such as glycine, antioxidants, bacteriostats, chelating agents such as EDTA or glutathione, adjuvants (*e.g.*, aluminum hydroxide), solutes that render the formulation isotonic, hypotonic or weakly hypertonic with the blood of a recipient, suspending agents, thickening agents and/or preservatives. Alternatively, compositions of the present invention may be formulated as a lyophilizate.

The pharmaceutical compositions described herein may be presented in unit-dose or multi-dose containers, such as sealed ampoules or vials. Such containers are typically sealed in such a way to preserve the sterility and stability of the formulation until use. In general, formulations may be stored as suspensions, solutions or emulsions in oily or aqueous vehicles. Alternatively, a pharmaceutical composition may be stored in a freeze-dried condition requiring only the addition of a sterile liquid carrier immediately prior to use.

The development of suitable dosing and treatment regimens for using the particular compositions described herein in a variety of treatment regimens, including *e.g.*, oral, parenteral, intravenous, intranasal, and intramuscular administration and formulation, is well known in the art, some of which are briefly discussed below for general purposes of illustration.

In certain applications, the pharmaceutical compositions disclosed herein may be delivered *via* oral administration to an animal. As such, these compositions may be formulated with an inert diluent or with an assimilable edible carrier, or they

may be enclosed in hard- or soft-shell gelatin capsule, or they may be compressed into tablets, or they may be incorporated directly with the food of the diet.

The active compounds may even be incorporated with excipients and used in the form of ingestible tablets, buccal tables, troches, capsules, elixirs, suspensions, syrups, wafers, and the like (see, for example, Mathiowitz *et al.*, Nature 5 1997 Mar 27;386(6623):410-4; Hwang *et al.*, Crit Rev Ther Drug Carrier Syst 1998;15(3):243-84; U. S. Patent 5,641,515; U. S. Patent 5,580,579 and U. S. Patent 5,792,451). Tablets, troches, pills, capsules and the like may also contain any of a variety of additional components, for example, a binder, such as gum tragacanth, acacia, 10 cornstarch, or gelatin; excipients, such as dicalcium phosphate; a disintegrating agent, such as corn starch, potato starch, alginic acid and the like; a lubricant, such as magnesium stearate; and a sweetening agent, such as sucrose, lactose or saccharin may be added or a flavoring agent, such as peppermint, oil of wintergreen, or cherry flavoring. When the dosage unit form is a capsule, it may contain, in addition to 15 materials of the above type, a liquid carrier. Various other materials may be present as coatings or to otherwise modify the physical form of the dosage unit. For instance, tablets, pills, or capsules may be coated with shellac, sugar, or both. Of course, any material used in preparing any dosage unit form should be pharmaceutically pure and substantially non-toxic in the amounts employed. In addition, the active compounds 20 may be incorporated into sustained-release preparation and formulations.

Typically, these formulations will contain at least about 0.1% of the active compound or more, although the percentage of the active ingredient(s) may, of course, be varied and may conveniently be between about 1 or 2% and about 60% or 70% or more of the weight or volume of the total formulation. Naturally, the amount of 25 active compound(s) in each therapeutically useful composition may be prepared is such a way that a suitable dosage will be obtained in any given unit dose of the compound. Factors such as solubility, bioavailability, biological half-life, route of administration, product shelf life, as well as other pharmacological considerations will be contemplated by one skilled in the art of preparing such pharmaceutical formulations, and as such, a 30 variety of dosages and treatment regimens may be desirable.



For oral administration, the compositions of the present invention may alternatively be incorporated with one or more excipients in the form of a mouthwash, dentifrice, buccal tablet, oral spray, or sublingual orally-administered formulation. Alternatively, the active ingredient may be incorporated into an oral solution such as one containing sodium borate, glycerin and potassium bicarbonate, or dispersed in a dentifrice, or added in a therapeutically-effective amount to a composition that may include water, binders, abrasives, flavoring agents, foaming agents, and humectants. Alternatively the compositions may be fashioned into a tablet or solution form that may be placed under the tongue or otherwise dissolved in the mouth.

In certain circumstances it will be desirable to deliver the pharmaceutical compositions disclosed herein parenterally, intravenously, intramuscularly, or even intraperitoneally. Such approaches are well known to the skilled artisan, some of which are further described, for example, in U. S. Patent 5,543,158; U. S. Patent 5,641,515 and U. S. Patent 5,399,363. In certain embodiments, solutions of the active compounds as free base or pharmacologically acceptable salts may be prepared in water suitably mixed with a surfactant, such as hydroxypropylcellulose. Dispersions may also be prepared in glycerol, liquid polyethylene glycols, and mixtures thereof and in oils. Under ordinary conditions of storage and use, these preparations generally will contain a preservative to prevent the growth of microorganisms.

Illustrative pharmaceutical forms suitable for injectable use include sterile aqueous solutions or dispersions and sterile powders for the extemporaneous preparation of sterile injectable solutions or dispersions (for example, see U. S. Patent 5,466,468). In all cases the form must be sterile and must be fluid to the extent that easy syringability exists. It must be stable under the conditions of manufacture and storage and must be preserved against the contaminating action of microorganisms, such as bacteria and fungi. The carrier can be a solvent or dispersion medium containing, for example, water, ethanol, polyol (e.g., glycerol, propylene glycol, and liquid polyethylene glycol, and the like), suitable mixtures thereof, and/or vegetable oils. Proper fluidity may be maintained, for example, by the use of a coating, such as lecithin, by the maintenance of the required particle size in the case of dispersion and/or

by the use of surfactants. The prevention of the action of microorganisms can be facilitated by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, sorbic acid, thimerosal, and the like. In many cases, it will be preferable to include isotonic agents, for example, sugars or sodium chloride.

- 5 Prolonged absorption of the injectable compositions can be brought about by the use in the compositions of agents delaying absorption, for example, aluminum monostearate and gelatin.

In one embodiment, for parenteral administration in an aqueous solution, the solution should be suitably buffered if necessary and the liquid diluent first rendered  
10 isotonic with sufficient saline or glucose. These particular aqueous solutions are especially suitable for intravenous, intramuscular, subcutaneous and intraperitoneal administration. In this connection, a sterile aqueous medium that can be employed will be known to those of skill in the art in light of the present disclosure. For example, one dosage may be dissolved in 1 ml of isotonic NaCl solution and either added to 1000 ml  
15 of hypodermoclysis fluid or injected at the proposed site of infusion, (see for example, "Remington's Pharmaceutical Sciences" 15th Edition, pages 1035-1038 and 1570-1580). Some variation in dosage will necessarily occur depending on the condition of the subject being treated. Moreover, for human administration, preparations will of course preferably meet sterility, pyrogenicity, and the general safety and purity  
20 standards as required by FDA Office of Biologics standards.

In another embodiment of the invention, the compositions disclosed herein may be formulated in a neutral or salt form. Illustrative pharmaceutically-acceptable salts include the acid addition salts (formed with the free amino groups of the protein) and which are formed with inorganic acids such as, for  
25 example, hydrochloric or phosphoric acids, or such organic acids as acetic, oxalic, tartaric, mandelic, and the like. Salts formed with the free carboxyl groups can also be derived from inorganic bases such as, for example, sodium, potassium, ammonium, calcium, or ferric hydroxides, and such organic bases as isopropylamine, trimethylamine, histidine, procaine and the like. Upon formulation, solutions will be

administered in a manner compatible with the dosage formulation and in such amount as is therapeutically effective.

The carriers can further comprise any and all solvents, dispersion media, vehicles, coatings, diluents, antibacterial and antifungal agents, isotonic and absorption  
5 delaying agents, buffers, carrier solutions, suspensions, colloids, and the like. The use of such media and agents for pharmaceutical active substances is well known in the art. Except insofar as any conventional media or agent is incompatible with the active ingredient, its use in the therapeutic compositions is contemplated. Supplementary active ingredients can also be incorporated into the compositions. The phrase  
10 "pharmaceutically-acceptable" refers to molecular entities and compositions that do not produce an allergic or similar untoward reaction when administered to a human.

In certain embodiments, the pharmaceutical compositions may be delivered by intranasal sprays, inhalation, and/or other aerosol delivery vehicles. Methods for delivering genes, nucleic acids, and peptide compositions directly to the  
15 lungs via nasal aerosol sprays has been described, *e.g.*, in U. S. Patent 5,756,353 and U. S. Patent 5,804,212. Likewise, the delivery of drugs using intranasal microparticle resins (Takenaga *et al.*, J Controlled Release 1998 Mar 2;52(1-2):81-7) and lysophosphatidyl-glycerol compounds (U. S. Patent 5,725,871) are also well-known in the pharmaceutical arts. Likewise, illustrative transmucosal drug delivery in the form of  
20 a polytetrafluoroethylene support matrix is described in U. S. Patent 5,780,045.

In certain embodiments, liposomes, nanocapsules, microparticles, lipid particles, vesicles, and the like, are used for the introduction of the compositions of the present invention into suitable host cells/organisms. In particular, the compositions of the present invention may be formulated for delivery either encapsulated in a lipid  
25 particle, a liposome, a vesicle, a nanosphere, or a nanoparticle or the like. Alternatively, compositions of the present invention can be bound, either covalently or non-covalently, to the surface of such carrier vehicles.

The formation and use of liposome and liposome-like preparations as potential drug carriers is generally known to those of skill in the art (see for example,  
30 Lasic, Trends Biotechnol 1998 Jul;16(7):307-21; Takakura, Nippon Rinsho 1998

Mar;56(3):691-5; Chandran *et al.*, Indian J Exp Biol. 1997 Aug;35(8):801-9; Margalit, Crit Rev Ther Drug Carrier Syst. 1995;12(2-3):233-61; U.S. Patent 5,567,434; U.S. Patent 5,552,157; U.S. Patent 5,565,213; U.S. Patent 5,738,868 and U.S. Patent 5,795,587, each specifically incorporated herein by reference in its entirety).

5               Liposomes have been used successfully with a number of cell types that are normally difficult to transfect by other procedures, including T cell suspensions, primary hepatocyte cultures and PC 12 cells (Renneisen *et al.*, J Biol Chem. 1990 Sep 25;265(27):16337-42; Muller *et al.*, DNA Cell Biol. 1990 Apr;9(3):221-9). In addition, liposomes are free of the DNA length constraints that are typical of viral-based delivery  
10 systems. Liposomes have been used effectively to introduce genes, various drugs, radiotherapeutic agents, enzymes, viruses, transcription factors, allosteric effectors and the like, into a variety of cultured cell lines and animals. Furthermore, the use of liposomes does not appear to be associated with autoimmune responses or unacceptable toxicity after systemic delivery.

15               In certain embodiments, liposomes are formed from phospholipids that are dispersed in an aqueous medium and spontaneously form multilamellar concentric bilayer vesicles (also termed multilamellar vesicles (MLVs)).

                  Alternatively, in other embodiments, the invention provides for pharmaceutically-acceptable nanocapsule formulations of the compositions of the  
20 present invention. Nanocapsules can generally entrap compounds in a stable and reproducible way (see, for example, Quintanar-Guerrero *et al.*, Drug Dev Ind Pharm. 1998 Dec;24(12):1113-28). To avoid side effects due to intracellular polymeric overloading, such ultrafine particles (sized around 0.1  $\mu$ m) may be designed using polymers able to be degraded *in vivo*. Such particles can be made as described, for  
25 example, by Couvreur *et al.*, Crit Rev Ther Drug Carrier Syst. 1988;5(1):1-20; zur Muhlen *et al.*, Eur J Pharm Biopharm. 1998 Mar;45(2):149-55; Zambaux *et al.* J Controlled Release. 1998 Jan 2;50(1-3):31-40; and U. S. Patent 5,145,684.

Cancer Therapeutic Methods

In further aspects of the present invention, the pharmaceutical compositions described herein may be used for the treatment of cancer, particularly for the immunotherapy of prostate cancer. Within such methods, the pharmaceutical compositions described herein are administered to a patient, typically a warm-blooded animal, preferably a human. A patient may or may not be afflicted with cancer. Accordingly, the above pharmaceutical compositions may be used to prevent the development of a cancer or to treat a patient afflicted with a cancer. Pharmaceutical compositions and vaccines may be administered either prior to or following surgical removal of primary tumors and/or treatment such as administration of radiotherapy or conventional chemotherapeutic drugs. As discussed above, administration of the pharmaceutical compositions may be by any suitable method, including administration by intravenous, intraperitoneal, intramuscular, subcutaneous, intranasal, intradermal, anal, vaginal, topical and oral routes.

Within certain embodiments, immunotherapy may be active immunotherapy, in which treatment relies on the *in vivo* stimulation of the endogenous host immune system to react against tumors with the administration of immune response-modifying agents (such as polypeptides and polynucleotides as provided herein).

Within other embodiments, immunotherapy may be passive immunotherapy, in which treatment involves the delivery of agents with established tumor-immune reactivity (such as effector cells or antibodies) that can directly or indirectly mediate antitumor effects and does not necessarily depend on an intact host immune system. Examples of effector cells include T cells as discussed above, T lymphocytes (such as CD8<sup>+</sup> cytotoxic T lymphocytes and CD4<sup>+</sup> T-helper tumor-infiltrating lymphocytes), killer cells (such as Natural Killer cells and lymphokine-activated killer cells), B cells and antigen-presenting cells (such as dendritic cells and macrophages) expressing a polypeptide provided herein. T cell receptors and antibody receptors specific for the polypeptides recited herein may be cloned, expressed and transferred into other vectors or effector cells for adoptive immunotherapy. The

polypeptides provided herein may also be used to generate antibodies or anti-idiotypic antibodies (as described above and in U.S. Patent No. 4,918,164) for passive immunotherapy.

Effector cells may generally be obtained in sufficient quantities for adoptive immunotherapy by growth *in vitro*, as described herein. Culture conditions for expanding single antigen-specific effector cells to several billion in number with retention of antigen recognition *in vivo* are well known in the art. Such *in vitro* culture conditions typically use intermittent stimulation with antigen, often in the presence of cytokines (such as IL-2) and non-dividing feeder cells. As noted above, immunoreactive polypeptides as provided herein may be used to rapidly expand antigen-specific T cell cultures in order to generate a sufficient number of cells for immunotherapy. In particular, antigen-presenting cells, such as dendritic, macrophage, monocyte, fibroblast and/or B cells, may be pulsed with immunoreactive polypeptides or transfected with one or more polynucleotides using standard techniques well known in the art. For example, antigen-presenting cells can be transfected with a polynucleotide having a promoter appropriate for increasing expression in a recombinant virus or other expression system. Cultured effector cells for use in therapy must be able to grow and distribute widely, and to survive long term *in vivo*. Studies have shown that cultured effector cells can be induced to grow *in vivo* and to survive long term in substantial numbers by repeated stimulation with antigen supplemented with IL-2 (*see, for example, Cheever et al., Immunological Reviews 157:177, 1997*).

Alternatively, a vector expressing a polypeptide recited herein may be introduced into antigen presenting cells taken from a patient and clonally propagated *ex vivo* for transplant back into the same patient. Transfected cells may be reintroduced into the patient using any means known in the art, preferably in sterile form by intravenous, intracavitary, intraperitoneal or intratumor administration.

Routes and frequency of administration of the therapeutic compositions described herein, as well as dosage, will vary from individual to individual, and may be readily established using standard techniques. In general, the pharmaceutical compositions and vaccines may be administered by injection (*e.g., intracutaneous,*

intramuscular, intravenous or subcutaneous), intranasally (*e.g.*, by aspiration) or orally. Preferably, between 1 and 10 doses may be administered over a 52 week period. Preferably, 6 doses are administered, at intervals of 1 month, and booster vaccinations may be given periodically thereafter. Alternate protocols may be appropriate for individual patients. A suitable dose is an amount of a compound that, when administered as described above, is capable of promoting an anti-tumor immune response, and is at least 10-50% above the basal (*i.e.*, untreated) level. Such response can be monitored by measuring the anti-tumor antibodies in a patient or by vaccine-dependent generation of cytolytic effector cells capable of killing the patient's tumor cells *in vitro*. Such vaccines should also be capable of causing an immune response that leads to an improved clinical outcome (*e.g.*, more frequent remissions, complete or partial or longer disease-free survival) in vaccinated patients as compared to non-vaccinated patients. In general, for pharmaceutical compositions and vaccines comprising one or more polypeptides, the amount of each polypeptide present in a dose ranges from about 25  $\mu$ g to 5 mg per kg of host. Suitable dose sizes will vary with the size of the patient, but will typically range from about 0.1 mL to about 5 mL.

In general, an appropriate dosage and treatment regimen provides the active compound(s) in an amount sufficient to provide therapeutic and/or prophylactic benefit. Such a response can be monitored by establishing an improved clinical outcome (*e.g.*, more frequent remissions, complete or partial, or longer disease-free survival) in treated patients as compared to non-treated patients. Increases in preexisting immune responses to a tumor protein generally correlate with an improved clinical outcome. Such immune responses may generally be evaluated using standard proliferation, cytotoxicity or cytokine assays, which may be performed using samples obtained from a patient before and after treatment.

#### Cancer Detection and Diagnostic Compositions, Methods and Kits

In general, a cancer may be detected in a patient based on the presence of one or more prostate tumor proteins and/or polynucleotides encoding such proteins in a biological sample (for example, blood, sera, sputum urine and/or tumor biopsies)

obtained from the patient. In other words, such proteins may be used as markers to indicate the presence or absence of a cancer such as prostate cancer. In addition, such proteins may be useful for the detection of other cancers. The binding agents provided herein generally permit detection of the level of antigen that binds to the agent in the  
5 biological sample. Polynucleotide primers and probes may be used to detect the level of mRNA encoding a tumor protein, which is also indicative of the presence or absence of a cancer. In general, a prostate tumor sequence should be present at a level that is at least three fold higher in tumor tissue than in normal tissue

There are a variety of assay formats known to those of ordinary skill in  
10 the art for using a binding agent to detect polypeptide markers in a sample. *See, e.g.,* Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In general, the presence or absence of a cancer in a patient may be determined by (a) contacting a biological sample obtained from a patient with a binding agent; (b) detecting in the sample a level of polypeptide that binds to the binding agent; and (c)  
15 comparing the level of polypeptide with a predetermined cut-off value.

In a preferred embodiment, the assay involves the use of binding agent immobilized on a solid support to bind to and remove the polypeptide from the remainder of the sample. The bound polypeptide may then be detected using a detection reagent that contains a reporter group and specifically binds to the binding  
20 agent/polypeptide complex. Such detection reagents may comprise, for example, a binding agent that specifically binds to the polypeptide or an antibody or other agent that specifically binds to the binding agent, such as an anti-immunoglobulin, protein G, protein A or a lectin. Alternatively, a competitive assay may be utilized, in which a polypeptide is labeled with a reporter group and allowed to bind to the immobilized  
25 binding agent after incubation of the binding agent with the sample. The extent to which components of the sample inhibit the binding of the labeled polypeptide to the binding agent is indicative of the reactivity of the sample with the immobilized binding agent. Suitable polypeptides for use within such assays include full length prostate tumor proteins and polypeptide portions thereof to which the binding agent binds, as  
30 described above.



The solid support may be any material known to those of ordinary skill in the art to which the tumor protein may be attached. For example, the solid support may be a test well in a microtiter plate or a nitrocellulose or other suitable membrane. Alternatively, the support may be a bead or disc, such as glass, fiberglass, latex or a plastic material such as polystyrene or polyvinylchloride. The support may also be a magnetic particle or a fiber optic sensor, such as those disclosed, for example, in U.S. Patent No. 5,359,681. The binding agent may be immobilized on the solid support using a variety of techniques known to those of skill in the art, which are amply described in the patent and scientific literature. In the context of the present invention, the term "immobilization" refers to both noncovalent association, such as adsorption, and covalent attachment (which may be a direct linkage between the agent and functional groups on the support or may be a linkage by way of a cross-linking agent). Immobilization by adsorption to a well in a microtiter plate or to a membrane is preferred. In such cases, adsorption may be achieved by contacting the binding agent, in a suitable buffer, with the solid support for a suitable amount of time. The contact time varies with temperature, but is typically between about 1 hour and about 1 day. In general, contacting a well of a plastic microtiter plate (such as polystyrene or polyvinylchloride) with an amount of binding agent ranging from about 10 ng to about 10  $\mu$ g, and preferably about 100 ng to about 1  $\mu$ g, is sufficient to immobilize an adequate amount of binding agent.

Covalent attachment of binding agent to a solid support may generally be achieved by first reacting the support with a bifunctional reagent that will react with both the support and a functional group, such as a hydroxyl or amino group, on the binding agent. For example, the binding agent may be covalently attached to supports having an appropriate polymer coating using benzoquinone or by condensation of an aldehyde group on the support with an amine and an active hydrogen on the binding partner (*see, e.g.*, Pierce Immunotechnology Catalog and Handbook, 1991, at A12-A13).

In certain embodiments, the assay is a two-antibody sandwich assay. This assay may be performed by first contacting an antibody that has been immobilized

on a solid support, commonly the well of a microtiter plate, with the sample, such that polypeptides within the sample are allowed to bind to the immobilized antibody. Unbound sample is then removed from the immobilized polypeptide-antibody complexes and a detection reagent (preferably a second antibody capable of binding to a different site on the polypeptide) containing a reporter group is added. The amount of  
5 detection reagent that remains bound to the solid support is then determined using a method appropriate for the specific reporter group.

More specifically, once the antibody is immobilized on the support as described above, the remaining protein binding sites on the support are typically  
10 blocked. Any suitable blocking agent known to those of ordinary skill in the art, such as bovine serum albumin or Tween 20™ (Sigma Chemical Co., St. Louis, MO). The immobilized antibody is then incubated with the sample, and polypeptide is allowed to bind to the antibody. The sample may be diluted with a suitable diluent, such as phosphate-buffered saline (PBS) prior to incubation. In general, an appropriate contact  
15 time (*i.e.*, incubation time) is a period of time that is sufficient to detect the presence of polypeptide within a sample obtained from an individual with prostate cancer. Preferably, the contact time is sufficient to achieve a level of binding that is at least about 95% of that achieved at equilibrium between bound and unbound polypeptide. Those of ordinary skill in the art will recognize that the time necessary to achieve  
20 equilibrium may be readily determined by assaying the level of binding that occurs over a period of time. At room temperature, an incubation time of about 30 minutes is generally sufficient.

Unbound sample may then be removed by washing the solid support with an appropriate buffer, such as PBS containing 0.1% Tween 20™. The second  
25 antibody, which contains a reporter group, may then be added to the solid support. Preferred reporter groups include those groups recited above.

The detection reagent is then incubated with the immobilized antibody-polypeptide complex for an amount of time sufficient to detect the bound polypeptide. An appropriate amount of time may generally be determined by assaying the level of  
30 binding that occurs over a period of time. Unbound detection reagent is then removed

and bound detection reagent is detected using the reporter group. The method employed for detecting the reporter group depends upon the nature of the reporter group. For radioactive groups, scintillation counting or autoradiographic methods are generally appropriate. Spectroscopic methods may be used to detect dyes, luminescent groups and fluorescent groups. Biotin may be detected using avidin, coupled to a different reporter group (commonly a radioactive or fluorescent group or an enzyme). Enzyme reporter groups may generally be detected by the addition of substrate (generally for a specific period of time), followed by spectroscopic or other analysis of the reaction products.

To determine the presence or absence of a cancer, such as prostate cancer, the signal detected from the reporter group that remains bound to the solid support is generally compared to a signal that corresponds to a predetermined cut-off value. In one preferred embodiment, the cut-off value for the detection of a cancer is the average mean signal obtained when the immobilized antibody is incubated with samples from patients without the cancer. In general, a sample generating a signal that is three standard deviations above the predetermined cut-off value is considered positive for the cancer. In an alternate preferred embodiment, the cut-off value is determined using a Receiver Operator Curve, according to the method of Sackett et al., *Clinical Epidemiology: A Basic Science for Clinical Medicine*, Little Brown and Co., 1985, p. 106-7. Briefly, in this embodiment, the cut-off value may be determined from a plot of pairs of true positive rates (*i.e.*, sensitivity) and false positive rates (100%-specificity) that correspond to each possible cut-off value for the diagnostic test result. The cut-off value on the plot that is the closest to the upper left-hand corner (*i.e.*, the value that encloses the largest area) is the most accurate cut-off value, and a sample generating a signal that is higher than the cut-off value determined by this method may be considered positive. Alternatively, the cut-off value may be shifted to the left along the plot, to minimize the false positive rate, or to the right, to minimize the false negative rate. In general, a sample generating a signal that is higher than the cut-off value determined by this method is considered positive for a cancer.

In a related embodiment, the assay is performed in a flow-through or strip test format, wherein the binding agent is immobilized on a membrane, such as nitrocellulose. In the flow-through test, polypeptides within the sample bind to the immobilized binding agent as the sample passes through the membrane. A second, 5 labeled binding agent then binds to the binding agent-polypeptide complex as a solution containing the second binding agent flows through the membrane. The detection of bound second binding agent may then be performed as described above. In the strip test format, one end of the membrane to which binding agent is bound is immersed in a solution containing the sample. The sample migrates along the membrane through a 10 region containing second binding agent and to the area of immobilized binding agent. Concentration of second binding agent at the area of immobilized antibody indicates the presence of a cancer. Typically, the concentration of second binding agent at that site generates a pattern, such as a line, that can be read visually. The absence of such a pattern indicates a negative result. In general, the amount of binding agent immobilized 15 on the membrane is selected to generate a visually discernible pattern when the biological sample contains a level of polypeptide that would be sufficient to generate a positive signal in the two-antibody sandwich assay, in the format discussed above. Preferred binding agents for use in such assays are antibodies and antigen-binding fragments thereof. Preferably, the amount of antibody immobilized on the membrane 20 ranges from about 25 ng to about 1  $\mu$ g, and more preferably from about 50 ng to about 500 ng. Such tests can typically be performed with a very small amount of biological sample.

Of course, numerous other assay protocols exist that are suitable for use with the tumor proteins or binding agents of the present invention. The above 25 descriptions are intended to be exemplary only. For example, it will be apparent to those of ordinary skill in the art that the above protocols may be readily modified to use tumor polypeptides to detect antibodies that bind to such polypeptides in a biological sample. The detection of such tumor protein specific antibodies may correlate with the presence of a cancer.

A cancer may also, or alternatively, be detected based on the presence of T cells that specifically react with a tumor protein in a biological sample. Within certain methods, a biological sample comprising CD4<sup>+</sup> and/or CD8<sup>+</sup> T cells isolated from a patient is incubated with a tumor polypeptide, a polynucleotide encoding such a polypeptide and/or an APC that expresses at least an immunogenic portion of such a polypeptide, and the presence or absence of specific activation of the T cells is detected. Suitable biological samples include, but are not limited to, isolated T cells. For example, T cells may be isolated from a patient by routine techniques (such as by Ficoll/Hypaque density gradient centrifugation of peripheral blood lymphocytes). T cells may be incubated *in vitro* for 2-9 days (typically 4 days) at 37°C with polypeptide (e.g., 5 - 25 µg/ml). It may be desirable to incubate another aliquot of a T cell sample in the absence of tumor polypeptide to serve as a control. For CD4<sup>+</sup> T cells, activation is preferably detected by evaluating proliferation of the T cells. For CD8<sup>+</sup> T cells, activation is preferably detected by evaluating cytolytic activity. A level of proliferation that is at least two fold greater and/or a level of cytolytic activity that is at least 20% greater than in disease-free patients indicates the presence of a cancer in the patient.

As noted above, a cancer may also, or alternatively, be detected based on the level of mRNA encoding a tumor protein in a biological sample. For example, at least two oligonucleotide primers may be employed in a polymerase chain reaction (PCR) based assay to amplify a portion of a tumor cDNA derived from a biological sample, wherein at least one of the oligonucleotide primers is specific for (*i.e.*, hybridizes to) a polynucleotide encoding the tumor protein. The amplified cDNA is then separated and detected using techniques well known in the art, such as gel electrophoresis. Similarly, oligonucleotide probes that specifically hybridize to a polynucleotide encoding a tumor protein may be used in a hybridization assay to detect the presence of polynucleotide encoding the tumor protein in a biological sample.

To permit hybridization under assay conditions, oligonucleotide primers and probes should comprise an oligonucleotide sequence that has at least about 60%, preferably at least about 75% and more preferably at least about 90%, identity to a portion of a polynucleotide encoding a tumor protein of the invention that is at least 10

nucleotides, and preferably at least 20 nucleotides, in length. Preferably, oligonucleotide primers and/or probes hybridize to a polynucleotide encoding a polypeptide described herein under moderately stringent conditions, as defined above. Oligonucleotide primers and/or probes which may be usefully employed in the  
5 diagnostic methods described herein preferably are at least 10-40 nucleotides in length. In a preferred embodiment, the oligonucleotide primers comprise at least 10 contiguous nucleotides, more preferably at least 15 contiguous nucleotides, of a DNA molecule having a sequence as disclosed herein. Techniques for both PCR based assays and hybridization assays are well known in the art (*see*, for example, Mullis et al., *Cold*  
10 *Spring Harbor Symp. Quant. Biol.*, 51:263, 1987; Erlich ed., *PCR Technology*, Stockton Press, NY, 1989).

One preferred assay employs RT-PCR, in which PCR is applied in conjunction with reverse transcription. Typically, RNA is extracted from a biological sample, such as biopsy tissue, and is reverse transcribed to produce cDNA molecules.  
15 PCR amplification using at least one specific primer generates a cDNA molecule, which may be separated and visualized using, for example, gel electrophoresis. Amplification may be performed on biological samples taken from a test patient and from an individual who is not afflicted with a cancer. The amplification reaction may be performed on several dilutions of cDNA spanning two orders of magnitude. A two-fold  
20 or greater increase in expression in several dilutions of the test patient sample as compared to the same dilutions of the non-cancerous sample is typically considered positive.

In another embodiment, the compositions described herein may be used as markers for the progression of cancer. In this embodiment, assays as described above  
25 for the diagnosis of a cancer may be performed over time, and the change in the level of reactive polypeptide(s) or polynucleotide(s) evaluated. For example, the assays may be performed every 24-72 hours for a period of 6 months to 1 year, and thereafter performed as needed. In general, a cancer is progressing in those patients in whom the level of polypeptide or polynucleotide detected increases over time. In contrast, the

cancer is not progressing when the level of reactive polypeptide or polynucleotide either remains constant or decreases with time.

Certain *in vivo* diagnostic assays may be performed directly on a tumor. One such assay involves contacting tumor cells with a binding agent. The bound  
5 binding agent may then be detected directly or indirectly via a reporter group. Such binding agents may also be used in histological applications. Alternatively, polynucleotide probes may be used within such applications.

As noted above, to improve sensitivity, multiple tumor protein markers may be assayed within a given sample. It will be apparent that binding agents specific  
10 for different proteins provided herein may be combined within a single assay. Further, multiple primers or probes may be used concurrently. The selection of tumor protein markers may be based on routine experiments to determine combinations that results in optimal sensitivity. In addition, or alternatively, assays for tumor proteins provided herein may be combined with assays for other known tumor antigens.

15 The present invention further provides kits for use within any of the above diagnostic methods. Such kits typically comprise two or more components necessary for performing a diagnostic assay. Components may be compounds, reagents, containers and/or equipment. For example, one container within a kit may contain a monoclonal antibody or fragment thereof that specifically binds to a tumor protein.  
20 Such antibodies or fragments may be provided attached to a support material, as described above. One or more additional containers may enclose elements, such as reagents or buffers, to be used in the assay. Such kits may also, or alternatively, contain a detection reagent as described above that contains a reporter group suitable for direct or indirect detection of antibody binding.

25 Alternatively, a kit may be designed to detect the level of mRNA encoding a tumor protein in a biological sample. Such kits generally comprise at least one oligonucleotide probe or primer, as described above, that hybridizes to a polynucleotide encoding a tumor protein. Such an oligonucleotide may be used, for example, within a PCR or hybridization assay. Additional components that may be

present within such kits include a second oligonucleotide and/or a diagnostic reagent or container to facilitate the detection of a polynucleotide encoding a tumor protein.

The following Examples are offered by way of illustration and not by way of limitation.



EXAMPLES

## EXAMPLE 1

## 5 ISOLATION AND CHARACTERIZATION OF PROSTATE-SPECIFIC POLYPEPTIDES

This Example describes the isolation of certain prostate-specific polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library was constructed from  
10 prostate tumor poly A<sup>+</sup> RNA using a Superscript Plasmid System for cDNA Synthesis and Plasmid Cloning kit (BRL Life Technologies, Gaithersburg, MD 20897) following the manufacturer's protocol. Specifically, prostate tumor tissues were homogenized with polytron (Kinematica, Switzerland) and total RNA was extracted using Trizol reagent (BRL Life Technologies) as directed by the manufacturer. The poly A<sup>+</sup> RNA  
15 was then purified using a Qiagen oligotex spin column mRNA purification kit (Qiagen, Santa Clarita, CA 91355) according to the manufacturer's protocol. First-strand cDNA was synthesized using the NotI/Oligo-dT18 primer. Double-stranded cDNA was synthesized, ligated with EcoRI/BAXI adaptors (Invitrogen, San Diego, CA) and digested with NotI. Following size fractionation with Chroma Spin-1000 columns  
20 (Clontech, Palo Alto, CA), the cDNA was ligated into the EcoRI/NotI site of pCDNA3.1 (Invitrogen) and transformed into ElectroMax *E. coli* DH10B cells (BRL Life Technologies) by electroporation.

Using the same procedure, a normal human pancreas cDNA expression library was prepared from a pool of six tissue specimens (Clontech). The cDNA  
25 libraries were characterized by determining the number of independent colonies, the percentage of clones that carried insert, the average insert size and by sequence analysis. The prostate tumor library contained  $1.64 \times 10^7$  independent colonies, with 70% of clones having an insert and the average insert size being 1745 base pairs. The normal pancreas cDNA library contained  $3.3 \times 10^6$  independent colonies, with 69% of clones  
30 having inserts and the average insert size being 1120 base pairs. For both libraries,

sequence analysis showed that the majority of clones had a full length cDNA sequence and were synthesized from mRNA, with minimal rRNA and mitochondrial DNA contamination.

cDNA library subtraction was performed using the above prostate tumor  
5 and normal pancreas cDNA libraries, as described by Hara *et al.* (*Blood*, 84:189-199, 1994) with some modifications. Specifically, a prostate tumor-specific subtracted cDNA library was generated as follows. Normal pancreas cDNA library (70 µg) was digested with EcoRI, NotI, and SfuI, followed by a filling-in reaction with DNA polymerase Klenow fragment. After phenol-chloroform extraction and ethanol  
10 precipitation, the DNA was dissolved in 100 µl of H<sub>2</sub>O, heat-denatured and mixed with 100 µl (100 µg) of Photoprobe biotin (Vector Laboratories, Burlingame, CA). As recommended by the manufacturer, the resulting mixture was irradiated with a 270 W sunlamp on ice for 20 minutes. Additional Photoprobe biotin (50 µl) was added and the biotinylation reaction was repeated. After extraction with butanol five times, the  
15 DNA was ethanol-precipitated and dissolved in 23 µl H<sub>2</sub>O to form the driver DNA.

To form the tracer DNA, 10 µg prostate tumor cDNA library was digested with BamHI and XhoI, phenol chloroform extracted and passed through Chroma spin-400 columns (Clontech). Following ethanol precipitation, the tracer DNA was dissolved in 5 µl H<sub>2</sub>O. Tracer DNA was mixed with 15 µl driver DNA and 20 µl of  
20 2 x hybridization buffer (1.5 M NaCl/10 mM EDTA/50 mM HEPES pH 7.5/0.2% sodium dodecyl sulfate), overlaid with mineral oil, and heat-denatured completely. The sample was immediately transferred into a 68 °C water bath and incubated for 20 hours (long hybridization [LH]). The reaction mixture was then subjected to a streptavidin treatment followed by phenol/chloroform extraction. This process was repeated three  
25 more times. Subtracted DNA was precipitated, dissolved in 12 µl H<sub>2</sub>O, mixed with 8 µl driver DNA and 20 µl of 2 x hybridization buffer, and subjected to a hybridization at 68 °C for 2 hours (short hybridization [SH]). After removal of biotinylated double-stranded DNA, subtracted cDNA was ligated into BamHI/XhoI site of chloramphenicol resistant pBCSK<sup>+</sup> (Stratagene, La Jolla, CA 92037) and transformed into ElectroMax *E.*

*coli* DH10B cells by electroporation to generate a prostate tumor specific subtracted cDNA library (referred to as "prostate subtraction 1").

To analyze the subtracted cDNA library, plasmid DNA was prepared from 100 independent clones, randomly picked from the subtracted prostate tumor specific library and grouped based on insert size. Representative cDNA clones were further characterized by DNA sequencing with a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A (Foster City, CA). Six cDNA clones, hereinafter referred to as F1-13, F1-12, F1-16, H1-1, H1-9 and H1-4, were shown to be abundant in the subtracted prostate-specific cDNA library. The determined 3' and 5' cDNA sequences for F1-12 are provided in SEQ ID NO: 2 and 3, respectively, with determined 3' cDNA sequences for F1-13, F1-16, H1-1, H1-9 and H1-4 being provided in SEQ ID NO: 1 and 4-7, respectively.

The cDNA sequences for the isolated clones were compared to known sequences in the gene bank using the EMBL and GenBank databases (release 96). Four of the prostate tumor cDNA clones, F1-13, F1-16, H1-1, and H1-4, were determined to encode the following previously identified proteins: prostate specific antigen (PSA), human glandular kallikrein, human tumor expression enhanced gene, and mitochondria cytochrome C oxidase subunit II. H1-9 was found to be identical to a previously identified human autonomously replicating sequence. No significant homologies to the cDNA sequence for F1-12 were found.

Subsequent studies led to the isolation of a full-length cDNA sequence for F1-12 (also referred to as P504S). This sequence is provided in SEQ ID NO: 107, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 108. cDNA splice variants of P504S are provided in SEQ ID NO: 600-605.

To clone less abundant prostate tumor specific genes, cDNA library subtraction was performed by subtracting the prostate tumor cDNA library described above with the normal pancreas cDNA library and with the three most abundant genes in the previously subtracted prostate tumor specific cDNA library: human glandular kallikrein, prostate specific antigen (PSA), and mitochondria cytochrome C oxidase subunit II. Specifically, 1 µg each of human glandular kallikrein, PSA and

mitochondria cytochrome C oxidase subunit II cDNAs in pCDNA3.1 were added to the driver DNA and subtraction was performed as described above to provide a second subtracted cDNA library hereinafter referred to as the "subtracted prostate tumor specific cDNA library with spike".

- 5                   Twenty-two cDNA clones were isolated from the subtracted prostate tumor specific cDNA library with spike. The determined 3' and 5' cDNA sequences for the clones referred to as J1-17, L1-12, N1-1862, J1-13, J1-19, J1-25, J1-24, K1-58, K1-63, L1-4 and L1-14 are provided in SEQ ID NOS: 8-9, 10-11, 12-13, 14-15, 16-17, 18-19, 20-21, 22-23, 24-25, 26-27 and 28-29, respectively. The determined 3' cDNA
- 10 sequences for the clones referred to as J1-12, J1-16, J1-21, K1-48, K1-55, L1-2, L1-6, N1-1858, N1-1860, N1-1861, N1-1864 are provided in SEQ ID NOS: 30-40, respectively. Comparison of these sequences with those in the gene bank as described above, revealed no significant homologies to three of the five most abundant DNA species, (J1-17, L1-12 and N1-1862; SEQ ID NOS: 8-9, 10-11 and 12-13, respectively).
- 15 Of the remaining two most abundant species, one (J1-12; SEQ ID NO:30) was found to be identical to the previously identified human pulmonary surfactant-associated protein, and the other (K1-48; SEQ ID NO:33) was determined to have some homology to *R. norvegicus* mRNA for 2-arylpropionyl-CoA epimerase. Of the 17 less abundant cDNA clones isolated from the subtracted prostate tumor specific cDNA library with spike,
- 20 four (J1-16, K1-55, L1-6 and N1-1864; SEQ ID NOS:31, 34, 36 and 40, respectively) were found to be identical to previously identified sequences, two (J1-21 and N1-1860; SEQ ID NOS: 32 and 38, respectively) were found to show some homology to non-human sequences, and two (L1-2 and N1-1861; SEQ ID NOS: 35 and 39, respectively) were found to show some homology to known human sequences. No significant
- 25 homologies were found to the polypeptides J1-13, J1-19, J1-24, J1-25, K1-58, K1-63, L1-4, L1-14 (SEQ ID NOS: 14-15, 16-17, 20-21, 18-19, 22-23, 24-25, 26-27, 28-29, respectively).

Subsequent studies led to the isolation of full length cDNA sequences for J1-17, L1-12 and N1-1862 (SEQ ID NOS: 109-111, respectively). The corresponding

predicted amino acid sequences are provided in SEQ ID NOS: 112-114. L1-12 is also referred to as P501S. A cDNA splice variant of P501S is provided in SEQ ID NO: 606.

In a further experiment, four additional clones were identified by subtracting a prostate tumor cDNA library with normal prostate cDNA prepared from a pool of three normal prostate poly A+ RNA (referred to as "prostate subtraction 2"). The determined cDNA sequences for these clones, hereinafter referred to as U1-3064, U1-3065, V1-3692 and 1A-3905, are provided in SEQ ID NO: 69-72, respectively. Comparison of the determined sequences with those in the gene bank revealed no significant homologies to U1-3065.

10 A second subtraction with spike (referred to as "prostate subtraction spike 2") was performed by subtracting a prostate tumor specific cDNA library with spike with normal pancreas cDNA library and further spiked with PSA, J1-17, pulmonary surfactant-associated protein, mitochondrial DNA, cytochrome c oxidase subunit II, N1-1862, autonomously replicating sequence, L1-12 and tumor expression enhanced gene. Four additional clones, hereinafter referred to as V1-3686, R1-2330, 1B-3976 and V1-3679, were isolated. The determined cDNA sequences for these clones are provided in SEQ ID NO:73-76, respectively. Comparison of these sequences with those in the gene bank revealed no significant homologies to V1-3686 and R1-2330.

20 Further analysis of the three prostate subtractions described above (prostate subtraction 2, subtracted prostate tumor specific cDNA library with spike, and prostate subtraction spike 2) resulted in the identification of sixteen additional clones, referred to as 1G-4736, 1G-4738, 1G-4741, 1G-4744, 1G-4734, 1H-4774, 1H-4781, 1H-4785, 1H-4787, 1H-4796, 1I-4810, 1I-4811, 1J-4876, 1K-4884 and 1K-4896. The determined cDNA sequences for these clones are provided in SEQ ID NOS: 77-92, respectively. Comparison of these sequences with those in the gene bank as described above, revealed no significant homologies to 1G-4741, 1G-4734, 1I-4807, 1J-4876 and 1K-4896 (SEQ ID NOS: 79, 81, 87, 90 and 92, respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1G-4736, 1G-4738, 1G-4741, 1G-4744, 1H-4774, 1H-4781, 1H-4785, 1H-4787, 1H-4796, 1I-4807,

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1J-4876, 1K-4884 and 1K-4896, provided in SEQ ID NOS: 179-188 and 191-193, respectively, and to the determination of additional partial cDNA sequences for 1I-4810 and 1I-4811, provided in SEQ ID NOS: 189 and 190, respectively.

Additional studies with prostate subtraction spike 2 resulted in the  
5 isolation of three more clones. Their sequences were determined as described above and compared to the most recent GenBank. All three clones were found to have homology to known genes, which are Cysteine-rich protein, KIAA0242, and KIAA0280 (SEQ ID NO: 317, 319, and 320, respectively). Further analysis of these clones by Synteni microarray (Synteni, Palo Alto, CA) demonstrated that all three clones were  
10 over-expressed in most prostate tumors and prostate BPH, as well as in the majority of normal prostate tissues tested, but low expression in all other normal tissues.

An additional subtraction was performed by subtracting a normal prostate cDNA library with normal pancreas cDNA (referred to as "prostate subtraction 3"). This led to the identification of six additional clones referred to as 1G-4761, 1G-  
15 4762, 1H-4766, 1H-4770, 1H-4771 and 1H-4772 (SEQ ID NOS: 93-98). Comparison of these sequences with those in the gene bank revealed no significant homologies to 1G-4761 and 1H-4771 (SEQ ID NOS: 93 and 97, respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1G-4761, 1G-4762, 1H-4766 and 1H-4772 provided in SEQ ID NOS: 194-196 and 199, respectively,  
20 and to the determination of additional partial cDNA sequences for 1H-4770 and 1H-4771, provided in SEQ ID NOS: 197 and 198, respectively.

Subtraction of a prostate tumor cDNA library, prepared from a pool of polyA+ RNA from three prostate cancer patients, with a normal pancreas cDNA library (prostate subtraction 4) led to the identification of eight clones, referred to as 1D-4297,  
25 1D-4309, 1D.1-4278, 1D-4288, 1D-4283, 1D-4304, 1D-4296 and 1D-4280 (SEQ ID NOS: 99-107). These sequences were compared to those in the gene bank as described above. No significant homologies were found to 1D-4283 and 1D-4304 (SEQ ID NOS: 103 and 104, respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1D-4309, 1D.1-4278, 1D-4288, 1D-

4283, 1D-4304, 1D-4296 and 1D-4280, provided in SEQ ID NOS: 200-206, respectively.

cDNA clones isolated in prostate subtraction 1 and prostate subtraction 2, described above, were colony PCR amplified and their mRNA expression levels in prostate tumor, normal prostate and in various other normal tissues were determined using microarray technology (Synteni, Palo Alto, CA). Briefly, the PCR amplification products were dotted onto slides in an array format, with each product occupying a unique location in the array. mRNA was extracted from the tissue sample to be tested, reverse transcribed, and fluorescent-labeled cDNA probes were generated. The microarrays were probed with the labeled cDNA probes, the slides scanned and fluorescence intensity was measured. This intensity correlates with the hybridization intensity. Two clones (referred to as P509S and P510S) were found to be over-expressed in prostate tumor and normal prostate and expressed at low levels in all other normal tissues tested (liver, pancreas, skin, bone marrow, brain, breast, adrenal gland, bladder, testes, salivary gland, large intestine, kidney, ovary, lung, spinal cord, skeletal muscle and colon). The determined cDNA sequences for P509S and P510S are provided in SEQ ID NO: 223 and 224, respectively. Comparison of these sequences with those in the gene bank as described above, revealed some homology to previously identified ESTs.

Additional studies led to the isolation of the full-length cDNA sequence for P509S. This sequence is provided in SEQ ID NO: 332, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 339. Two variant full-length cDNA sequences for P510S are provided in SEQ ID NO: 535 and 536, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 537 and 538, respectively. Additional splice variants of P510S are provided in SEQ ID NO: 598 and 599.

The determined cDNA sequences for additional prostate-specific clones isolated during characterization of prostate specific cDNA libraries are provided in SEQ ID NO: 618-689, 691-697 and 709-772. Comparison of these sequences with those in the public databases revealed no significant homologies to any of these sequences.

## EXAMPLE 2

## DETERMINATION OF TISSUE SPECIFICITY OF PROSTATE-SPECIFIC POLYPEPTIDES

5           Using gene specific primers, mRNA expression levels for the representative prostate-specific polypeptides F1-16, H1-1, J1-17 (also referred to as P502S), L1-12 (also referred to as P501S), F1-12 (also referred to as P504S) and N1-1862 (also referred to as P503S) were examined in a variety of normal and tumor tissues using RT-PCR.

10           Briefly, total RNA was extracted from a variety of normal and tumor tissues using Trizol reagent as described above. First strand synthesis was carried out using 1-2 µg of total RNA with SuperScript II reverse transcriptase (BRL Life Technologies) at 42 °C for one hour. The cDNA was then amplified by PCR with gene-specific primers. To ensure the semi-quantitative nature of the RT-PCR, β-actin was  
15           used as an internal control for each of the tissues examined. First, serial dilutions of the first strand cDNAs were prepared and RT-PCR assays were performed using β-actin specific primers. A dilution was then chosen that enabled the linear range amplification of the β-actin template and which was sensitive enough to reflect the differences in the initial copy numbers. Using these conditions, the β-actin levels were determined for  
20           each reverse transcription reaction from each tissue. DNA contamination was minimized by DNase treatment and by assuring a negative PCR result when using first strand cDNA that was prepared without adding reverse transcriptase.

          mRNA Expression levels were examined in four different types of tumor tissue (prostate tumor from 2 patients, breast tumor from 3 patients, colon tumor, lung  
25           tumor), and sixteen different normal tissues, including prostate, colon, kidney, liver, lung, ovary, pancreas, skeletal muscle, skin, stomach, testes, bone marrow and brain. F1-16 was found to be expressed at high levels in prostate tumor tissue, colon tumor and normal prostate, and at lower levels in normal liver, skin and testes, with expression being undetectable in the other tissues examined. H1-1 was found to be expressed at  
30           high levels in prostate tumor, lung tumor, breast tumor, normal prostate, normal colon



and normal brain, at much lower levels in normal lung, pancreas, skeletal muscle, skin, small intestine, bone marrow, and was not detected in the other tissues tested. J1-17 (P502S) and L1-12 (P501S) appear to be specifically over-expressed in prostate, with both genes being expressed at high levels in prostate tumor and normal prostate but at low to undetectable levels in all the other tissues examined. N1-1862 (P503S) was found to be over-expressed in 60% of prostate tumors and detectable in normal colon and kidney. The RT-PCR results thus indicate that F1-16, H1-1, J1-17 (P502S), N1-1862 (P503S) and L1-12 (P501S) are either prostate specific or are expressed at significantly elevated levels in prostate.

Further RT-PCR studies showed that F1-12 (P504S) is over-expressed in 60% of prostate tumors, detectable in normal kidney but not detectable in all other tissues tested. Similarly, R1-2330 was shown to be over-expressed in 40% of prostate tumors, detectable in normal kidney and liver, but not detectable in all other tissues tested. U1-3064 was found to be over-expressed in 60% of prostate tumors, and also expressed in breast and colon tumors, but was not detectable in normal tissues.

RT-PCR characterization of R1-2330, U1-3064 and 1D-4279 showed that these three antigens are over-expressed in prostate and/or prostate tumors.

Northern analysis with four prostate tumors, two normal prostate samples, two BPH prostates, and normal colon, kidney, liver, lung, pancreas, skeletal muscle, brain, stomach, testes, small intestine and bone marrow, showed that L1-12 (P501S) is over-expressed in prostate tumors and normal prostate, while being undetectable in other normal tissues tested. J1-17 (P502S) was detected in two prostate tumors and not in the other tissues tested. N1-1862 (P503S) was found to be over-expressed in three prostate tumors and to be expressed in normal prostate, colon and kidney, but not in other tissues tested. F1-12 (P504S) was found to be highly expressed in two prostate tumors and to be undetectable in all other tissues tested.

The microarray technology described above was used to determine the expression levels of representative antigens described herein in prostate tumor, breast tumor and the following normal tissues: prostate, liver, pancreas, skin, bone marrow, brain, breast, adrenal gland, bladder, testes, salivary gland, large intestine, kidney,

ovary, lung, spinal cord, skeletal muscle and colon. L1-12 (P501S) was found to be over-expressed in normal prostate and prostate tumor, with some expression being detected in normal skeletal muscle. Both J1-12 and F1-12 (P504S) were found to be over-expressed in prostate tumor, with expression being lower or undetectable in all other tissues tested. N1-1862 (P503S) was found to be expressed at high levels in prostate tumor and normal prostate, and at low levels in normal large intestine and normal colon, with expression being undetectable in all other tissues tested. R1-2330 was found to be over-expressed in prostate tumor and normal prostate, and to be expressed at lower levels in all other tissues tested. 1D-4279 was found to be over-expressed in prostate tumor and normal prostate, expressed at lower levels in normal spinal cord, and to be undetectable in all other tissues tested.

Further microarray analysis to specifically address the extent to which P501S (SEQ ID NO: 110) was expressed in breast tumor revealed moderate over-expression not only in breast tumor, but also in metastatic breast tumor (2/31), with negligible to low expression in normal tissues. This data suggests that P501S may be over-expressed in various breast tumors as well as in prostate tumors.

The expression levels of 32 ESTs (expressed sequence tags) described by Vasmatazis *et al.* (*Proc. Natl. Acad. Sci. USA* 95:300-304, 1998) in a variety of tumor and normal tissues were examined by microarray technology as described above. Two of these clones (referred to as P1000C and P1001C) were found to be over-expressed in prostate tumor and normal prostate, and expressed at low to undetectable levels in all other tissues tested (normal aorta, thymus, resting and activated PBMC, epithelial cells, spinal cord, adrenal gland, fetal tissues, skin, salivary gland, large intestine, bone marrow, liver, lung, dendritic cells, stomach, lymph nodes, brain, heart, small intestine, skeletal muscle, colon and kidney. The determined cDNA sequences for P1000C and P1001C are provided in SEQ ID NO: 384 and 472, respectively. The sequence of P1001C was found to show some homology to the previously isolated Human mRNA for JM27 protein. Subsequent comparison of the sequence of SEQ ID NO: 384 with sequences in the public databases, led to the identification of a full-length cDNA sequence of P1000C (SEQ ID NO: 929), which encodes a 492 amino acid sequence.

Analysis of the amino acid sequence using the PSORT II program led to the identification of a putative transmembrane domain from amino acids 84-100. The cDNA sequence of the open reading frame of P1000C, including the stop codon, is provided in SEQ ID NO: 930, with the open reading frame without the stop codon being  
5 provided in SEQ ID NO: 931. The full-length amino acid sequence of P1000C is provided in SEQ ID NO: 932. SEQ ID NO: 933 and 934 represent amino acids 1-100 and 100-492 of P1000C, respectively.

The expression of the polypeptide encoded by the full length cDNA sequence for F1-12 (also referred to as P504S; SEQ ID NO: 108) was investigated by  
10 immunohistochemical analysis. Rabbit-anti-P504S polyclonal antibodies were generated against the full length P504S protein by standard techniques. Subsequent isolation and characterization of the polyclonal antibodies were also performed by techniques well known in the art. Immunohistochemical analysis showed that the P504S polypeptide was expressed in 100% of prostate carcinoma samples tested (n=5).

15 The rabbit-anti-P504S polyclonal antibody did not appear to label benign prostate cells with the same cytoplasmic granular staining, but rather with light nuclear staining. Analysis of normal tissues revealed that the encoded polypeptide was found to be expressed in some, but not all normal human tissues. Positive cytoplasmic staining with rabbit-anti-P504S polyclonal antibody was found in normal human kidney, liver,  
20 brain, colon and lung-associated macrophages, whereas heart and bone marrow were negative.

This data indicates that the P504S polypeptide is present in prostate cancer tissues, and that there are qualitative and quantitative differences in the staining between benign prostatic hyperplasia tissues and prostate cancer tissues, suggesting that  
25 this polypeptide may be detected selectively in prostate tumors and therefore be useful in the diagnosis of prostate cancer.

## EXAMPLE 3

ISOLATION AND CHARACTERIZATION OF PROSTATE-SPECIFIC  
POLYPEPTIDES BY PCR-BASED SUBTRACTION

5 A cDNA subtraction library, containing cDNA from normal prostate subtracted with ten other normal tissue cDNAs (brain, heart, kidney, liver, lung, ovary, placenta, skeletal muscle, spleen and thymus) and then submitted to a first round of PCR amplification, was purchased from Clontech. This library was subjected to a second round of PCR amplification, following the manufacturer's protocol. The  
10 resulting cDNA fragments were subcloned into the vector pT7 Blue T-vector (Novagen, Madison, WI) and transformed into XL-1 Blue MRF' *E. coli* (Stratagene). DNA was isolated from independent clones and sequenced using a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A.

Fifty-nine positive clones were sequenced. Comparison of the DNA  
15 sequences of these clones with those in the gene bank, as described above, revealed no significant homologies to 25 of these clones, hereinafter referred to as P5, P8, P9, P18, P20, P30, P34, P36, P38, P39, P42, P49, P50, P53, P55, P60, P64, P65, P73, P75, P76, P79 and P84. The determined cDNA sequences for these clones are provided in SEQ ID NO: 41-45, 47-52 and 54-65, respectively. P29, P47, P68, P80 and P82 (SEQ ID  
20 NO: 46, 53 and 66-68, respectively) were found to show some degree of homology to previously identified DNA sequences. To the best of the inventors' knowledge, none of these sequences have been previously shown to be present in prostate.

Further studies employing the sequence of SEQ ID NO: 67 as a probe in standard full-length cloning methods, resulted in the isolation of three cDNA sequences  
25 which appear to be splice variants of P80 (also known as P704P). These sequences are provided in SEQ ID NO: 699-701.

Further studies using the PCR-based methodology described above resulted in the isolation of more than 180 additional clones, of which 23 clones were found to show no significant homologies to known sequences. The determined cDNA  
30 sequences for these clones are provided in SEQ ID NO: 115-123, 127, 131, 137, 145,

147-151, 153, 156-158 and 160. Twenty-three clones (SEQ ID NO: 124-126, 128-130, 132-136, 138-144, 146, 152, 154, 155 and 159) were found to show some homology to previously identified ESTs. An additional ten clones (SEQ ID NO: 161-170) were found to have some degree of homology to known genes. Larger cDNA clones  
5 containing the P20 sequence represent splice variants of a gene referred to as P703P. The determined DNA sequence for the variants referred to as DE1, DE13 and DE14 are provided in SEQ ID NOS: 171, 175 and 177, respectively, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 172, 176 and 178, respectively. The determined cDNA sequence for an extended spliced form of P703 is  
10 provided in SEQ ID NO: 225. The DNA sequences for the splice variants referred to as DE2 and DE6 are provided in SEQ ID NOS: 173 and 174, respectively.

mRNA Expression levels for representative clones in tumor tissues (prostate (n=5), breast (n=2), colon and lung) normal tissues (prostate (n=5), colon, kidney, liver, lung (n=2), ovary (n=2), skeletal muscle, skin, stomach, small intestine  
15 and brain), and activated and non-activated PBMC was determined by RT-PCR as described above. Expression was examined in one sample of each tissue type unless otherwise indicated.

P9 was found to be highly expressed in normal prostate and prostate tumor compared to all normal tissues tested except for normal colon which showed  
20 comparable expression. P20, a portion of the P703P gene, was found to be highly expressed in normal prostate and prostate tumor, compared to all twelve normal tissues tested. A modest increase in expression of P20 in breast tumor (n=2), colon tumor and lung tumor was seen compared to all normal tissues except lung (1 of 2). Increased expression of P18 was found in normal prostate, prostate tumor and breast tumor  
25 compared to other normal tissues except lung and stomach. A modest increase in expression of P5 was observed in normal prostate compared to most other normal tissues. However, some elevated expression was seen in normal lung and PBMC. Elevated expression of P5 was also observed in prostate tumors (2 of 5), breast tumor and one lung tumor sample. For P30, similar expression levels were seen in normal  
30 prostate and prostate tumor, compared to six of twelve other normal tissues tested.

Increased expression was seen in breast tumors, one lung tumor sample and one colon tumor sample, and also in normal PBMC. P29 was found to be over-expressed in prostate tumor (5 of 5) and normal prostate (5 of 5) compared to the majority of normal tissues. However, substantial expression of P29 was observed in normal colon and  
5 normal lung (2 of 2). P80 was found to be over-expressed in prostate tumor (5 of 5) and normal prostate (5 of 5) compared to all other normal tissues tested, with increased expression also being seen in colon tumor.

Further studies resulted in the isolation of twelve additional clones, hereinafter referred to as 10-d8, 10-h10, 11-c8, 7-g6, 8-b5, 8-b6, 8-d4, 8-d9, 8-g3, 8-  
10 h11, 9-f12 and 9-f3. The determined DNA sequences for 10-d8, 10-h10, 11-c8, 8-d4, 8-d9, 8-h11, 9-f12 and 9-f3 are provided in SEQ ID NO: 207, 208, 209, 216, 217, 220, 221 and 222, respectively. The determined forward and reverse DNA sequences for 7-g6, 8-b5, 8-b6 and 8-g3 are provided in SEQ ID NO: 210 and 211; 212 and 213; 214 and 215; and 218 and 219, respectively. Comparison of these sequences with those in  
15 the gene bank revealed no significant homologies to the sequence of 9-f3. The clones 10-d8, 11-c8 and 8-h11 were found to show some homology to previously isolated ESTs, while 10-h10, 8-b5, 8-b6, 8-d4, 8-d9, 8-g3 and 9-f12 were found to show some homology to previously identified genes. Further characterization of 7-G6 and 8-G3 showed identity to the known genes PAP and PSA, respectively.

20 mRNA expression levels for these clones were determined using the micro-array technology described above. The clones 7-G6, 8-G3, 8-B5, 8-B6, 8-D4, 8-D9, 9-F3, 9-F12, 9-H3, 10-A2, 10-A4, 11-C9 and 11-F2 were found to be over-expressed in prostate tumor and normal prostate, with expression in other tissues tested being low or undetectable. Increased expression of 8-F11 was seen in prostate tumor  
25 and normal prostate, bladder, skeletal muscle and colon. Increased expression of 10-H10 was seen in prostate tumor and normal prostate, bladder, lung, colon, brain and large intestine. Increased expression of 9-B1 was seen in prostate tumor, breast tumor, and normal prostate, salivary gland, large intestine and skin, with increased expression of 11-C8 being seen in prostate tumor, and normal prostate and large intestine.

An additional cDNA fragment derived from the PCR-based normal prostate subtraction, described above, was found to be prostate specific by both microarray technology and RT-PCR. The determined cDNA sequence of this clone (referred to as 9-A11) is provided in SEQ ID NO: 226. Comparison of this sequence with those  
5 in the public databases revealed 99% identity to the known gene HOXB13.

Further studies led to the isolation of the clones 8-C6 and 8-H7. The determined cDNA sequences for these clones are provided in SEQ ID NO: 227 and 228, respectively. These sequences were found to show some homology to previously isolated ESTs.

10 PCR and hybridization-based methodologies were employed to obtain longer cDNA sequences for clone P20 (also referred to as P703P), yielding three additional cDNA fragments that progressively extend the 5' end of the gene. These fragments, referred to as P703PDE5, P703P6.26, and P703PX-23 (SEQ ID NO: 326, 328 and 330, with the predicted corresponding amino acid sequences being provided in  
15 SEQ ID NO: 327, 329 and 331, respectively) contain additional 5' sequence. P703PDE5 was recovered by screening of a cDNA library (#141-26) with a portion of P703P as a probe. P703P6.26 was recovered from a mixture of three prostate tumor cDNAs and P703PX\_23 was recovered from cDNA library (#438-48). Together, the additional sequences include all of the putative mature serine protease along with part of  
20 the putative signal sequence. The full-length cDNA sequence for P703P is provided in SEQ ID NO: 524, with the corresponding amino acid sequence being provided in SEQ ID NO: 525.

Using computer algorithms, the following regions of P703P were predicted to represent potential HLA A2-binding CTL epitopes: amino acids 164-172  
25 of SEQ ID NO: 525 (SEQ ID NO: 866); amino acids 160-168 of SEQ ID NO: 525 (SEQ ID NO: 867); amino acids 239-247 of SEQ ID NO: 525 (SEQ ID NO: 868); amino acids 118-126 of SEQ ID NO: 525 (SEQ ID NO: 869); amino acids 112-120 of SEQ ID NO: 525 (SEQ ID NO: 870); amino acids 155-164 of SEQ ID NO: 525 (SEQ ID NO: 871); amino acids 117-126 of SEQ ID NO: 525 (SEQ ID NO: 872); amino acids  
30 164-173 of SEQ ID NO: 525 (SEQ ID NO: 873); amino acids 154-163 of SEQ ID NO:

525 (SEQ ID NO: 874); amino acids 163-172 of SEQ ID NO: 525 (SEQ ID NO: 875); amino acids 58-66 of SEQ ID NO: 525 (SEQ ID NO: 876); and amino acids 59-67 of SEQ ID NO: 525 (SEQ ID NO: 877).

P703P was found to show some homology to previously identified proteases, such as thrombin. The thrombin receptor has been shown to be preferentially expressed in highly metastatic breast carcinoma cells and breast carcinoma biopsy samples. Introduction of thrombin receptor antisense cDNA has been shown to inhibit the invasion of metastatic breast carcinoma cells in culture. Antibodies against thrombin receptor inhibit thrombin receptor activation and thrombin-induced platelet activation. Furthermore, peptides that resemble the receptor's tethered ligand domain inhibit platelet aggregation by thrombin. P703P may play a role in prostate cancer through a protease-activated receptor on the cancer cell or on stromal cells. The potential trypsin-like protease activity of P703P may either activate a protease-activated receptor on the cancer cell membrane to promote tumorigenesis or activate a protease-activated receptor on the adjacent cells (such as stromal cells) to secrete growth factors and/or proteases (such as matrix metalloproteinases) that could promote tumor angiogenesis, invasion and metastasis. P703P may thus promote tumor progression and/or metastasis through the activation of protease-activated receptor. Polypeptides and antibodies that block the P703P-receptor interaction may therefore be usefully employed in the treatment of prostate cancer.

To determine whether P703P expression increases with increased severity of Gleason grade, an indicator of tumor stage, quantitative PCR analysis was performed on prostate tumor samples with a range of Gleason scores from 5 to > 8. The mean level of P703P expression increased with increasing Gleason score, indicating that P703P expression may correlate with increased disease severity.

Further studies using a PCR-based subtraction library of a prostate tumor pool subtracted against a pool of normal tissues (referred to as JP: PCR subtraction) resulted in the isolation of thirteen additional clones, seven of which did not share any significant homology to known GenBank sequences. The determined cDNA sequences for these seven clones (P711P, P712P, novel 23, P774P, P775P, P710P and P768P) are



provided in SEQ ID NO: 307-311, 313 and 315, respectively. The remaining six clones (SEQ ID NO: 316 and 321-325) were shown to share some homology to known genes. By microarray analysis, all thirteen clones showed three or more fold over-expression in prostate tissues, including prostate tumors, BPH and normal prostate as compared to  
5 normal non-prostate tissues. Clones P711P, P712P, novel 23 and P768P showed over-expression in most prostate tumors and BPH tissues tested (n=29), and in the majority of normal prostate tissues (n=4), but background to low expression levels in all normal tissues. Clones P774P, P775P and P710P showed comparatively lower expression and expression in fewer prostate tumors and BPH samples, with negative to low expression  
10 in normal prostate.

Further studies led to the isolation of an extended cDNA sequence for P712P (SEQ ID NO: 552). The amino acid sequences encoded by 16 predicted open reading frames present within the sequence of SEQ ID NO: 552 are provided in SEQ ID NO: 553-568.

15 The full-length cDNA for P711P was obtained by employing the partial sequence of SEQ ID NO: 307 to screen a prostate cDNA library. Specifically, a directionally cloned prostate cDNA library was prepared using standard techniques. One million colonies of this library were plated onto LB/Amp plates. Nylon membrane filters were used to lift these colonies, and the cDNAs which were picked up by these  
20 filters were denatured and cross-linked to the filters by UV light. The P711P cDNA fragment of SEQ ID NO: 307 was radio-labeled and used to hybridize with these filters. Positive clones were selected, and cDNAs were prepared and sequenced using an automatic Perkin Elmer/Applied Biosystems sequencer. The determined full-length sequence of P711P is provided in SEQ ID NO: 382, with the corresponding predicted  
25 amino acid sequence being provided in SEQ ID NO: 383.

Using PCR and hybridization-based methodologies, additional cDNA sequence information was derived for two clones described above, 11-C9 and 9-F3, herein after referred to as P707P and P714P, respectively (SEQ ID NO: 333 and 334). After comparison with the most recent GenBank, P707P was found to be a splice  
30 variant of the known gene HoxB13. In contrast, no significant homologies to P714P

were found. Further studies employing the sequence of SEQ ID NO: 334 as a probe in standard full-length cloning methods, resulted in an extended cDNA sequence for P714P. This sequence is provided in SEQ ID NO: 698. This sequence was found to show some homology to the gene that encodes human ribosomal L23A protein.

5 Clones 8-B3, P89, P98, P130 and P201 (as disclosed in U.S. Patent Application No. 09/020,956, filed February 9, 1998) were found to be contained within one contiguous sequence, referred to as P705P (SEQ ID NO: 335, with the predicted amino acid sequence provided in SEQ ID NO: 336), which was determined to be a splice variant of the known gene NKX 3.1.

10 Further studies on P775P resulted in the isolation of four additional sequences (SEQ ID NO: 473-476) which are all splice variants of the P775P gene. The sequence of SEQ ID NO: 474 was found to contain two open reading frames (ORFs). The predicted amino acid sequences encoded by these ORFs are provided in SEQ ID NO: 477 and 478. The cDNA sequence of SEQ ID NO: 475 was found to contain an  
15 ORF which encodes the amino acid sequence of SEQ ID NO: 479. The cDNA sequence of SEQ ID NO: 473 was found to contain four ORFs. The predicted amino acid sequences encoded by these ORFs are provided in SEQ ID NO: 480-483. Additional splice variants of P775P are provided in SEQ ID NO: 593-597.

Subsequent studies led to the identification of a genomic region on  
20 chromosome 22q11.2, known as the Cat Eye Syndrome region, that contains the five prostate genes P704P, P712P, P774P, P775P and B305D. The relative location of each of these five genes within the genomic region is shown in Fig. 10. This region may therefore be associated with malignant tumors, and other potential tumor genes may be contained within this region. These studies also led to the identification of a potential  
25 open reading frame (ORF) for P775P (provided in SEQ ID NO: 533), which encodes the amino acid sequence of SEQ ID NO: 534.

Comparison of the clone of SEQ ID NO: 325 (referred to as P558S) with sequences in the GenBank and GeneSeq DNA databases showed that P558S is identical to the prostate-specific transglutaminase gene, which is known to have two forms. The  
30 full-length sequences for the two forms are provided in SEQ ID NO: 773 and 774, with

the corresponding amino acid sequences being provided in SEQ ID NO: 775 and 776, respectively. The cDNA sequence of SEQ ID NO: 774 has a 15 pair base insert, resulting in a 5 amino acid insert in the corresponding amino acid sequence (SEQ ID NO: 776). This insert is not present in the sequence of SEQ ID NO: 773.

5 Further studies on P768P (SEQ ID NO: 315) led to the identification of the putative full-length open reading frame (ORF). The cDNA sequence of the ORF with stop codon is provided in SEQ ID NO: 907. The cDNA sequence of the ORF without stop codon is provided in SEQ ID NO: 908, with the corresponding amino acid sequence being provided in SEQ ID NO: 909. This sequence was found to show 86%  
10 identity to a rat calcium transporter protein, indicating that P768P may represent a human calcium transporter protein. The locations of transmembrane domains within P768P were predicted using the PSORT II computer algorithm. Six transmembrane domains were predicted at amino acid positions 118-134, 172-188, 211-227, 230-246, 282-298 and 348-364. The amino acid sequences of SEQ ID NO: 910-915 represent  
15 amino acids 1-134, 135-188, 189-227, 228-246, 247-298 and 299-511 of P768P, respectively.

#### EXAMPLE 4

##### SYNTHESIS OF POLYPEPTIDES

20

Polypeptides may be synthesized on a Perkin Elmer/Applied Biosystems 430A peptide synthesizer using Fmoc chemistry with HPTU (O-Benzotriazole-N,N,N',N'-tetramethyluronium hexafluorophosphate) activation. A Gly-Cys-Gly sequence may be attached to the amino terminus of the peptide to provide a method of  
25 conjugation, binding to an immobilized surface, or labeling of the peptide. Cleavage of the peptides from the solid support may be carried out using the following cleavage mixture: trifluoroacetic acid:ethanedithiol:thioanisole:water:phenol (40:1:2:2:3). After cleaving for 2 hours, the peptides may be precipitated in cold methyl-t-butyl-ether. The peptide pellets may then be dissolved in water containing 0.1% trifluoroacetic acid  
30 (TFA) and lyophilized prior to purification by C18 reverse phase HPLC. A gradient of

0%-60% acetonitrile (containing 0.1% TFA) in water (containing 0.1% TFA) may be used to elute the peptides. Following lyophilization of the pure fractions, the peptides may be characterized using electrospray or other types of mass spectrometry and by amino acid analysis.

5

## EXAMPLE 5

FURTHER ISOLATION AND CHARACTERIZATION OF  
PROSTATE-SPECIFIC POLYPEPTIDES BY PCR-BASED SUBTRACTION

10 A cDNA library generated from prostate primary tumor mRNA as described above was subtracted with cDNA from normal prostate. The subtraction was performed using a PCR-based protocol (Clontech), which was modified to generate larger fragments. Within this protocol, tester and driver double stranded cDNA were separately digested with five restriction enzymes that recognize six-nucleotide  
15 restriction sites (MluI, MscI, PvuII, SalI and StuI). This digestion resulted in an average cDNA size of 600 bp, rather than the average size of 300 bp that results from digestion with RsaI according to the Clontech protocol. This modification did not affect the subtraction efficiency. Two tester populations were then created with different adapters, and the driver library remained without adapters.

20 The tester and driver libraries were then hybridized using excess driver cDNA. In the first hybridization step, driver was separately hybridized with each of the two tester cDNA populations. This resulted in populations of (a) unhybridized tester cDNAs, (b) tester cDNAs hybridized to other tester cDNAs, (c) tester cDNAs hybridized to driver cDNAs and (d) unhybridized driver cDNAs. The two separate  
25 hybridization reactions were then combined, and rehybridized in the presence of additional denatured driver cDNA. Following this second hybridization, in addition to populations (a) through (d), a fifth population (e) was generated in which tester cDNA with one adapter hybridized to tester cDNA with the second adapter. Accordingly, the second hybridization step resulted in enrichment of differentially expressed sequences  
30 which could be used as templates for PCR amplification with adaptor-specific primers.

The ends were then filled in, and PCR amplification was performed using adaptor-specific primers. Only population (e), which contained tester cDNA that did not hybridize to driver cDNA, was amplified exponentially. A second PCR amplification step was then performed, to reduce background and further enrich  
5 differentially expressed sequences.

This PCR-based subtraction technique normalizes differentially expressed cDNAs so that rare transcripts that are overexpressed in prostate tumor tissue may be recoverable. Such transcripts would be difficult to recover by traditional subtraction methods.

10 In addition to genes known to be overexpressed in prostate tumor, seventy-seven further clones were identified. Sequences of these partial cDNAs are provided in SEQ ID NO: 29 to 305. Most of these clones had no significant homology to database sequences. Exceptions were JPTPN23 (SEQ ID NO: 231; similarity to pig valosin-containing protein), JPTPN30 (SEQ ID NO: 234; similarity to rat mRNA for  
15 proteasome subunit), JPTPN45 (SEQ ID NO: 243; similarity to rat *norvegicus* cytosolic NADP-dependent isocitrate dehydrogenase), JPTPN46 (SEQ ID NO: 244; similarity to human subclone H8 4 d4 DNA sequence), JP1D6 (SEQ ID NO: 265; similarity to *G. gallus* dynein light chain-A), JP8D6 (SEQ ID NO: 288; similarity to human BAC clone RG016J04), JP8F5 (SEQ ID NO: 289; similarity to human subclone H8 3 b5 DNA  
20 sequence), and JP8E9 (SEQ ID NO: 299; similarity to human Alu sequence).

Additional studies using the PCR-based subtraction library consisting of a prostate tumor pool subtracted against a normal prostate pool (referred to as PT-PN PCR subtraction) yielded three additional clones. Comparison of the cDNA sequences of these clones with the most recent release of GenBank revealed no significant  
25 homologies to the two clones referred to as P715P and P767P (SEQ ID NO: 312 and 314). The remaining clone was found to show some homology to the known gene KIAA0056 (SEQ ID NO: 318). Using microarray analysis to measure mRNA expression levels in various tissues, all three clones were found to be over-expressed in prostate tumors and BPH tissues. Specifically, clone P715P was over-expressed in most  
30 prostate tumors and BPH tissues by a factor of three or greater, with elevated expression

seen in the majority of normal prostate samples and in fetal tissue, but negative to low expression in all other normal tissues. Clone P767P was over-expressed in several prostate tumors and BPH tissues, with moderate expression levels in half of the normal prostate samples, and background to low expression in all other normal tissues tested.

5 Further analysis, by microarray as described above, of the PT-PN PCR subtraction library and of a DNA subtraction library containing cDNA from prostate tumor subtracted with a pool of normal tissue cDNAs, led to the isolation of 27 additional clones (SEQ ID NO: 340-365 and 381) which were determined to be over-expressed in prostate tumor. The clones of SEQ ID NO: 341, 342, 345, 347, 348, 349,  
10 351, 355-359, 361, 362 and 364 were also found to be expressed in normal prostate. Expression of all 26 clones in a variety of normal tissues was found to be low or undetectable, with the exception of P544S (SEQ ID NO: 356) which was found to be expressed in small intestine. Of the 26 clones, 11 (SEQ ID NO: 340-349 and 362) were found to show some homology to previously identified sequences. No significant  
15 homologies were found to the clones of SEQ ID NO: 350, 351, 353-361, and 363-365.

Comparison of the sequence of SEQ ID NO: 362 with sequences in the GenBank and GeneSeq DNA databases showed that this clone (referred to as P788P) is identical to GeneSeq Accession No. X27262, which encodes a protein found in the GeneSeq protein Accession No. Y00931. The full length cDNA sequence of P788P is  
20 shown in Figure 12A (SEQ ID NO: 777), with the corresponding predicted amino acid being shown in Figure 12B (SEQ ID NO: 778). Subsequently, a full-length cDNA sequence for P788P that contains polymorphisms not found in the sequence of SEQ ID NO: 779, was cloned multiple times by PCR amplification from cDNA prepared from several RNA templates from three individuals. This determined cDNA sequence of this  
25 polymorphic variant of P788P is provided in SEQ ID NO: 779, with the corresponding amino acid sequence being provided in SEQ ID NO: 780. The sequence of SEQ ID NO: 780 differs from that of SEQ ID NO: 778 by six amino acid residues. The P788P protein has 7 potential transmembrane domains at the C-terminal portion and is predicted to be a plasma membrane protein with an extracellular N-terminal region.

Further studies on the clone of SEQ ID NO: 352 (referred to as P790P) led to the isolation of the full-length cDNA sequence of SEQ ID NO: 526. The corresponding predicted amino acid is provided in SEQ ID NO: 527. Data from two quantitative PCR experiments indicated that P790P is over-expressed in 11/15 tested prostate tumor samples and is expressed at low levels in spinal cord, with no expression being seen in all other normal samples tested. Data from further PCR experiments and microarray experiments showed over-expression in normal prostate and prostate tumor with little or no expression in other tissues tested. P790P was subsequently found to show significant homology to a previously identified G-protein coupled prostate tissue receptor.

Additional studies on the clone of SEQ ID NO: 354 (referred to as P776P) led to the isolation of an extended cDNA sequence, provided in SEQ ID NO: 569. The determined cDNA sequences of three additional splice variants of P776P are provided in SEQ ID NO: 570-572. The amino acid sequences encoded by two predicted open reading frames (ORFs) contained within SEQ ID NO: 570, one predicted ORF contained within SEQ ID NO: 571, and 11 predicted ORFs contained within SEQ ID NO: 569, are provided in SEQ ID NO: 573-586, respectively. Further studies led to the isolation of the full-length sequence for the clone of SEQ ID NO: 570 (provided in SEQ ID NO: 880). Full-length cloning efforts on the clone of SEQ ID NO: 571 led to the isolation of two sequences (provided in SEQ ID NO: 881 and 882), representing a single clone, that are identical with the exception of a polymorphic insertion/deletion at position 1293. Specifically, the clone of SEQ ID NO: 882 (referred to as clone F1) has a C at position 1293. The clone of SEQ ID NO: 881 (referred to as clone F2) has a single base pair deletion at position 1293. The predicted amino acid sequences encoded by 5 open reading frames located within SEQ ID NO: 880 are provided in SEQ ID NO: 883-887, with the predicted amino acid sequences encoded by the clone of SEQ ID NO: 881 and 882 being provided in SEQ ID NO: 888-893.

Comparison of the cDNA sequences for the clones P767P (SEQ ID NO: 314) and P777P (SEQ ID NO: 350) with sequences in the GenBank human EST database showed that the two clones matched many EST sequences in common,

suggesting that P767P and P777P may represent the same gene. A DNA consensus sequence derived from a DNA sequence alignment of P767P, P777P and multiple EST clones is provided in SEQ ID NO: 587. The amino acid sequences encoded by three putative ORFs located within SEQ ID NO: 587 are provided in SEQ ID NO: 588-590.

5           The clone of SEQ ID NO: 342 (referred to as P789P) was found to show homology to a previously identified gene. The full length cDNA sequence for P789P and the corresponding amino acid sequence are provided in SEQ ID NO: 878 and 879, respectively.

10

## EXAMPLE 6

## PEPTIDE PRIMING OF MICE AND PROPAGATION OF CTL LINES

6.1. This Example illustrates the preparation of a CTL cell line specific for cells expressing the P502S gene.

15           Mice expressing the transgene for human HLA A2Kb (provided by Dr L. Sherman, The Scripps Research Institute, La Jolla, CA) were immunized with P2S#12 peptide (VLGWVAEL; SEQ ID NO: 306), which is derived from the P502S gene (also referred to herein as J1-17, SEQ ID NO: 8), as described by Theobald et al., *Proc. Natl. Acad. Sci. USA* 92:11993-11997, 1995 with the following modifications. Mice were  
20 immunized with 100µg of P2S#12 and 120µg of an I-A<sup>b</sup> binding peptide derived from hepatitis B Virus protein emulsified in incomplete Freund's adjuvant. Three weeks later these mice were sacrificed and using a nylon mesh single cell suspensions prepared. Cells were then resuspended at  $6 \times 10^6$  cells/ml in complete media (RPMI-1640; Gibco BRL, Gaithersburg, MD) containing 10% FCS, 2mM Glutamine (Gibco BRL), sodium  
25 pyruvate (Gibco BRL), non-essential amino acids (Gibco BRL),  $2 \times 10^{-5}$  M 2-mercaptoethanol, 50U/ml penicillin and streptomycin, and cultured in the presence of irradiated (3000 rads) P2S#12-pulsed (5mg/ml P2S#12 and 10mg/ml β2-microglobulin) LPS blasts (A2 transgenic spleens cells cultured in the presence of 7µg/ml dextran sulfate and 25µg/ml LPS for 3 days). Six days later, cells ( $5 \times 10^5$ /ml) were  
30 restimulated with  $2.5 \times 10^6$ /ml peptide pulsed irradiated (20,000 rads) EL4A2Kb cells



(Sherman et al, *Science* 258:815-818, 1992) and  $3 \times 10^6$ /ml A2 transgenic spleen feeder cells. Cells were cultured in the presence of 20U/ml IL-2. Cells continued to be restimulated on a weekly basis as described, in preparation for cloning the line.

P2S#12 line was cloned by limiting dilution analysis with peptide pulsed EL4 A2Kb tumor cells ( $1 \times 10^4$  cells/ well) as stimulators and A2 transgenic spleen cells as feeders ( $5 \times 10^5$  cells/ well) grown in the presence of 30U/ml IL-2. On day 14, cells were restimulated as before. On day 21, clones that were growing were isolated and maintained in culture. Several of these clones demonstrated significantly higher reactivity (lysis) against human fibroblasts (HLA A2Kb expressing) transduced with P502S than against control fibroblasts. An example is presented in Figure 1.

This data indicates that P2S #12 represents a naturally processed epitope of the P502S protein that is expressed in the context of the human HLA A2Kb molecule.

6.2. This Example illustrates the preparation of murine CTL lines and CTL clones specific for cells expressing the P501S gene.

This series of experiments were performed similarly to that described above. Mice were immunized with the P1S#10 peptide (SEQ ID NO: 337), which is derived from the P501S gene (also referred to herein as L1-12, SEQ ID NO: 110). The P1S#10 peptide was derived by analysis of the predicted polypeptide sequence for P501S for potential HLA-A2 binding sequences as defined by published HLA-A2 binding motifs (Parker, KC, et al, *J. Immunol.*, 152:163, 1994). P1S#10 peptide was synthesized as described in Example 4, and empirically tested for HLA-A2 binding using a T cell based competition assay. Predicted A2 binding peptides were tested for their ability to compete HLA-A2 specific peptide presentation to an HLA-A2 restricted CTL clone (D150M58), which is specific for the HLA-A2 binding influenza matrix peptide fluM58. D150M58 CTL secretes TNF in response to self-presentation of peptide fluM58. In the competition assay, test peptides at 100-200  $\mu$ g/ml were added to cultures of D150M58 CTL in order to bind HLA-A2 on the CTL. After thirty minutes,

CTL cultured with test peptides, or control peptides, were tested for their antigen dose response to the fluM58 peptide in a standard TNF bioassay. As shown in Figure 3, peptide P1S#10 competes HLA-A2 restricted presentation of fluM58, demonstrating that peptide P1S#10 binds HLA-A2.

5 Mice expressing the transgene for human HLA A2Kb were immunized as described by Theobald et al. (*Proc. Natl. Acad. Sci. USA* 92:11993-11997, 1995) with the following modifications. Mice were immunized with 62.5 $\mu$ g of P1S #10 and 120 $\mu$ g of an I-A<sup>b</sup> binding peptide derived from Hepatitis B Virus protein emulsified in incomplete Freund's adjuvant. Three weeks later these mice were sacrificed and single  
10 cell suspensions prepared using a nylon mesh. Cells were then resuspended at  $6 \times 10^6$  cells/ml in complete media (as described above) and cultured in the presence of irradiated (3000 rads) P1S#10-pulsed (2 $\mu$ g/ml P1S#10 and 10mg/ml  $\beta$ 2-microglobulin) LPS blasts (A2 transgenic spleens cells cultured in the presence of 7 $\mu$ g/ml dextran sulfate and 25 $\mu$ g/ml LPS for 3 days). Six days later cells ( $5 \times 10^5$ /ml) were restimulated  
15 with  $2.5 \times 10^6$ /ml peptide-pulsed irradiated (20,000 rads) EL4A2Kb cells, as described above, and  $3 \times 10^6$ /ml A2 transgenic spleen feeder cells. Cells were cultured in the presence of 20 U/ml IL-2. Cells were restimulated on a weekly basis in preparation for cloning. After three rounds of *in vitro* stimulations, one line was generated that recognized P1S#10-pulsed Jurkat A2Kb targets and P501S-transduced Jurkat targets as  
20 shown in Figure 4.

A P1S#10-specific CTL line was cloned by limiting dilution analysis with peptide pulsed EL4 A2Kb tumor cells ( $1 \times 10^4$  cells/ well) as stimulators and A2 transgenic spleen cells as feeders ( $5 \times 10^5$  cells/ well) grown in the presence of 30U/ml IL-2. On day 14, cells were restimulated as before. On day 21, viable clones were  
25 isolated and maintained in culture. As shown in Figure 5, five of these clones demonstrated specific cytolytic reactivity against P501S-transduced Jurkat A2Kb targets. This data indicates that P1S#10 represents a naturally processed epitope of the P501S protein that is expressed in the context of the human HLA-A2.1 molecule.

## EXAMPLE 7

PRIMING OF CTL *IN VIVO* USING NAKED DNA IMMUNIZATION  
WITH A PROSTATE ANTIGEN

The prostate-specific antigen L1-12, as described above, is also referred  
5 to as P501S. HLA A2Kb Tg mice (provided by Dr L. Sherman, The Scripps Research  
Institute, La Jolla, CA) were immunized with 100 µg P501S in the vector VR1012  
either intramuscularly or intradermally. The mice were immunized three times, with a  
two week interval between immunizations. Two weeks after the last immunization,  
immune spleen cells were cultured with Jurkat A2Kb-P501S transduced stimulator  
10 cells. CTL lines were stimulated weekly. After two weeks of *in vitro* stimulation, CTL  
activity was assessed against P501S transduced targets. Two out of 8 mice developed  
strong anti-P501S CTL responses. These results demonstrate that P501S contains at  
least one naturally processed HLA-A2-restricted CTL epitope.

15

## EXAMPLE 8

## ABILITY OF HUMAN T CELLS TO RECOGNIZE PROSTATE-SPECIFIC POLYPEPTIDES

This Example illustrates the ability of T cells specific for a prostate  
tumor polypeptide to recognize human tumor.

20 Human CD8<sup>+</sup> T cells were primed *in vitro* to the P2S-12 peptide (SEQ  
ID NO: 306) derived from P502S (also referred to as J1-17) using dendritic cells  
according to the protocol of Van Tsai et al. (*Critical Reviews in Immunology* 18:65-75,  
1998). The resulting CD8<sup>+</sup> T cell microcultures were tested for their ability to  
recognize the P2S-12 peptide presented by autologous fibroblasts or fibroblasts which  
25 were transduced to express the P502S gene in a γ-interferon ELISPOT assay (*see*  
Lalvani et al., *J. Exp. Med.* 186:859-865, 1997). Briefly, titrating numbers of T cells  
were assayed in duplicate on 10<sup>4</sup> fibroblasts in the presence of 3 µg/ml human β<sub>2</sub>-  
microglobulin and 1 µg/ml P2S-12 peptide or control E75 peptide. In addition, T cells  
were simultaneously assayed on autologous fibroblasts transduced with the P502S gene  
30 or as a control, fibroblasts transduced with HER-2/*neu*. Prior to the assay, the

fibroblasts were treated with 10 ng/ml  $\gamma$ -interferon for 48 hours to upregulate class I MHC expression. One of the microcultures (#5) demonstrated strong recognition of both peptide pulsed fibroblasts as well as transduced fibroblasts in a  $\gamma$ -interferon ELISPOT assay. Figure 2A demonstrates that there was a strong increase in the number of  $\gamma$ -interferon spots with increasing numbers of T cells on fibroblasts pulsed with the P2S-12 peptide (solid bars) but not with the control E75 peptide (open bars). This shows the ability of these T cells to specifically recognize the P2S-12 peptide. As shown in Figure 2B, this microculture also demonstrated an increase in the number of  $\gamma$ -interferon spots with increasing numbers of T cells on fibroblasts transduced to express the P502S gene but not the HER-2/*neu* gene. These results provide additional confirmatory evidence that the P2S-12 peptide is a naturally processed epitope of the P502S protein. Furthermore, this also demonstrates that there exists in the human T cell repertoire, high affinity T cells which are capable of recognizing this epitope. These T cells should also be capable of recognizing human tumors which express the P502S gene.

## EXAMPLE 9

### ELICITATION OF PROSTATE ANTIGEN-SPECIFIC CTL RESPONSES

#### IN HUMAN BLOOD

This Example illustrates the ability of a prostate-specific antigen to elicit a CTL response in blood of normal humans.

Autologous dendritic cells (DC) were differentiated from monocyte cultures derived from PBMC of normal donors by growth for five days in RPMI medium containing 10% human serum, 50 ng/ml GM-CSF and 30 ng/ml IL-4. Following culture, DC were infected overnight with recombinant P501S-expressing vaccinia virus at an M.O.I. of 5 and matured for 8 hours by the addition of 2 micrograms/ml CD40 ligand. Virus was inactivated by UV irradiation, CD8<sup>+</sup> cells were isolated by positive selection using magnetic beads, and priming cultures were initiated in 24-well plates. Following five stimulation cycles using autologous fibroblasts

retrovirally transduced to express P501S and CD80, CD8+ lines were identified that specifically produced interferon-gamma when stimulated with autologous P501S-transduced fibroblasts. The P501S-specific activity of cell line 3A-1 could be maintained following additional stimulation cycles on autologous B-LCL transduced with P501S. Line 3A-1 was shown to specifically recognize autologous B-LCL transduced to express P501S, but not EGFP-transduced autologous B-LCL, as measured by cytotoxicity assays ( $^{51}\text{Cr}$  release) and interferon-gamma production (Interferon-gamma Elispot; *see above and Lalvani et al., J. Exp. Med. 186:859-865, 1997*). The results of these assays are presented in Figures 6A and 6B.

10

## EXAMPLE 10

IDENTIFICATION OF A NATURALLY PROCESSED CTL EPITOPE CONTAINED WITHIN THE  
PROSTATE-SPECIFIC ANTIGEN P703P

The 9-mer peptide p5 (SEQ ID NO: 338) was derived from the P703P antigen (also referred to as P20). The p5 peptide is immunogenic in human HLA-A2 donors and is a naturally processed epitope. Antigen specific human CD8+ T cells can be primed following repeated *in vitro* stimulations with monocytes pulsed with p5 peptide. These CTL specifically recognize p5-pulsed and P703P-transduced target cells in both ELISPOT (as described above) and chromium release assays. Additionally, immunization of HLA-A2Kb transgenic mice with p5 leads to the generation of CTL lines which recognize a variety of HLA-A2Kb or HLA-A2 transduced target cells expressing P703P.

Initial studies demonstrating that p5 is a naturally processed epitope were done using HLA-A2Kb transgenic mice. HLA-A2Kb transgenic mice were immunized subcutaneously in the footpad with 100  $\mu\text{g}$  of p5 peptide together with 140  $\mu\text{g}$  of hepatitis B virus core peptide (a Th peptide) in Freund's incomplete adjuvant. Three weeks post immunization, spleen cells from immunized mice were stimulated *in vitro* with peptide-pulsed LPS blasts. CTL activity was assessed by chromium release assay five days after primary *in vitro* stimulation. Retrovirally transduced cells expressing the

control antigen P703P and HLA-A2Kb were used as targets. CTL lines that specifically recognized both p5-pulsed targets as well as P703P-expressing targets were identified.

Human *in vitro* priming experiments demonstrated that the p5 peptide is immunogenic in humans. Dendritic cells (DC) were differentiated from monocyte  
5 cultures derived from PBMC of normal human donors by culturing for five days in RPMI medium containing 10% human serum, 50 ng/ml human GM-CSF and 30 ng/ml human IL-4. Following culture, the DC were pulsed with 1 ug/ml p5 peptide and cultured with CD8+ T cell enriched PBMC. CTL lines were restimulated on a weekly basis with p5-pulsed monocytes. Five to six weeks after initiation of the CTL cultures,  
10 CTL recognition of p5-pulsed target cells was demonstrated. CTL were additionally shown to recognize human cells transduced to express P703P, demonstrating that p5 is a naturally processed epitope.

Studies identifying a further peptide epitope (referred to as peptide 4) derived from the prostate tumor-specific antigen P703P that is capable of being  
15 recognized by CD4 T cells on the surface of cells in the context of HLA class II molecules were carried out as follows. The amino acid sequence for peptide 4 is provided in SEQ ID NO: 781, with the corresponding cDNA sequence being provided in SEQ ID NO: 782.

Twenty 15-mer peptides overlapping by 10 amino acids and derived  
20 from the carboxy-terminal fragment of P703P were generated using standard procedures. Dendritic cells (DC) were derived from PBMC of a normal female donor using GM-CSF and IL-4 by standard protocols. CD4 T cells were generated from the same donor as the DC using MACS beads and negative selection. DC were pulsed overnight with pools of the 15-mer peptides, with each peptide at a final concentration  
25 of 0.25 microgram/ml. Pulsed DC were washed and plated at  $1 \times 10^4$  cells/well of 96-well V-bottom plates and purified CD4 T cells were added at  $1 \times 10^5$ /well. Cultures were supplemented with 60 ng/ml IL-6 and 10 ng/ml IL-12 and incubated at 37 °C. Cultures were restimulated as above on a weekly basis using DC generated and pulsed as above as antigen presenting cells, supplemented with 5 ng/ml IL-7 and 10 u/ml IL-2.  
30 Following 4 *in vitro* stimulation cycles, 96 lines (each line corresponding to one well) were tested for specific proliferation and cytokine production in response to the

stimulating pools with an irrelevant pool of peptides derived from mammaglobin being used as a control.

One line (referred to as 1-F9) was identified from pool #1 that demonstrated specific proliferation (measured by 3H proliferation assays) and cytokine production (measured by interferon-gamma ELISA assays) in response to pool #1 of P703P peptides. This line was further tested for specific recognition of the peptide pool, specific recognition of individual peptides in the pool, and in HLA mismatch analyses to identify the relevant restricting allele. Line 1-F9 was found to specifically proliferate and produce interferon-gamma in response to peptide pool #1, and also to peptide 4 (SEQ ID NO: 781). Peptide 4 corresponds to amino acids 126-140 of SEQ ID NO: 327. Peptide titration experiments were conducted to assess the sensitivity of line 1-F9 for the specific peptide. The line was found to specifically respond to peptide 4 at concentrations as low as 0.25 ng/ml, indicating that the T cells are very sensitive and therefore likely to have high affinity for the epitope.

To determine the HLA restriction of the P703P response, a panel of antigen presenting cells (APC) was generated that was partially matched with the donor used to generate the T cells. The APC were pulsed with the peptide and used in proliferation and cytokine assays together with line 1-F9. APC matched with the donor at HLA-DRB0701 and HLA-DQB02 alleles were able to present the peptide to the T cells, indicating that the P703P-specific response is restricted to one of these alleles.

Antibody blocking assays were utilized to determine if the restricting allele was HLA-DR0701 or HLA-DQ02. The anti-HLA-DR blocking antibody L243 or an irrelevant isotype matched IgG2a were added to T cells and APC cultures pulsed with the peptide RMPTVLQCVNVS VVS (SEQ ID NO: 781) at 250 ng/ml. Standard interferon-gamma and proliferation assays were performed. Whereas the control antibody had no effect on the ability of the T cells to recognize peptide-pulsed APC, in both assays the anti-HLA-DR antibody completely blocked the ability of the T cells to specifically recognize peptide-pulsed APC.

To determine if the peptide epitope RMPTVLQCVNVS VVS (SEQ ID NO: 781) was naturally processed, the ability of line 1-F9 to recognize APC pulsed with recombinant P703P protein was examined. For these experiments a number of

recombinant P703P sources were utilized; *E. coli*-derived P703P, Pichia-derived P703P and baculovirus-derived P703P. Irrelevant protein controls used were *E. coli*-derived L3E (a lung-specific antigen) and baculovirus-derived mammaglobin. In interferon-gamma ELISA assays, line 1-F9 was able to efficiently recognize both *E. coli* forms of P703P as well as Pichia-derived recombinant P703P, while baculovirus-derived P703P was recognized less efficiently. Subsequent Western blot analysis revealed that the *E. coli* and Pichia P703P protein preparations were intact while the baculovirus P703P preparation was approximately 75% degraded. Thus, peptide RMPTVLQCVNVS VVS (SEQ ID NO: 781) from P703P is a naturally processed peptide epitope derived from P703P and presented to T cells in the context of HLA-DRB-0701

In further studies, twenty-four 15-mer peptides overlapping by 10 amino acids and derived from the N-terminal fragment of P703P (corresponding to amino acids 27-154 of SEQ ID NO: 525) were generated by standard procedures and their ability to be recognized by CD4 cells was determined essentially as described above. DC were pulsed overnight with pools of the peptides with each peptide at a final concentration of 10 microgram/ml. A large number of individual CD4 T cell lines (65/480) demonstrated significant proliferation and cytokine release (IFN-gamma) in response to the P703P peptide pools but not to a control peptide pool. The CD4 T cell lines which demonstrated specific activity were restimulated on the appropriate pool of P703P peptides and reassayed on the individual peptides of each pool as well as a peptide dose titration of the pool of peptides in a IFN-gamma release assay and in a proliferation assay.

Sixteen immunogenic peptides were recognized by the T cells from the entire set of peptide antigens tested. The amino acid sequences of these peptides are provided in SEQ ID NO: 799-814, with the corresponding cDNA sequences being provided in SEQ ID NO: 783-798, respectively. In some cases the peptide reactivity of the T cell line could be mapped to a single peptide, however some could be mapped to more than one peptide in each pool. Those CD4 T cell lines that displayed a representative pattern of recognition from each peptide pool with a reasonable affinity for peptide were chosen for further analysis (I-1A, -6A; II-4C, -5E; III-6E, IV-4B, -3F, -9B, -10F, V-5B, -4D, and -10F). These CD4 T cells lines were restimulated on the



appropriate individual peptide and reassayed on autologous DC pulsed with a truncated form of recombinant P703P protein made in *E. coli* (a.a. 96 - 254 of SEQ ID NO: 525), full-length P703P made in the baculovirus expression system, and a fusion between influenza virus NS1 and P703P made in *E. coli*. Of the T cell lines tested, line I-1A  
5 recognized specifically the truncated form of P703P (*E. coli*) but no other recombinant form of P703P. This line also recognized the peptide used to elicit the T cells. Line 2-4C recognized the truncated form of P703P (*E. coli*) and the full length form of P703P made in baculovirus, as well as peptide. The remaining T cell lines tested were either peptide-specific only (II-5E, II-6F, IV-4B, IV-3F, IV-9B, IV-10F, V-5B and V-4D) or  
10 were non-responsive to any antigen tested (V-10F). These results demonstrate that the peptide sequence RPLLANDMLIKLDE (SEQ ID NO: 814; corresponding to a.a. 110-124 of SEQ ID NO: 525) recognized by the T cell line I-1A, and the peptide sequences SVSESDTIRSISIAS (SEQ ID NO: 811; corresponding to a.a. 125-139 of SEQ ID NO: 525) and ISIASQCPTAGNSCL (SEQ ID NO: 810; corresponding to a.a. 135-149 of  
15 SEQ ID NO: 525) recognized by the T cell line II-4C may be naturally processed epitopes of the P703P protein.

In further studies, forty 15-mer peptides overlapping by 10 amino acids and derived spanning amino acids 47 to 254 of P703P (SEQ ID NO: 525) were generated by standard procedures and their ability to be recognized by CD4 cells was  
20 determined essentially as described above. DC were prepared from PBMC of a donor having distinct HLA DR and DQ alleles from that used in previous experiments. DC were pulsed overnight with pools of the peptides with each peptide at a final concentration of 0.25 microgram/ml, and each pool containing 10 peptides. Twelve lines were identified that demonstrated specific proliferation and cytokine production  
25 (measured in gamma-interferon ELISA assays) in response to the stimulating peptide pool. These lines were further tested for specific recognition of the peptide pool, specific recognition of individual peptides in the pool, and specific recognition of recombinant P703P protein. Lines 3A5H and 3A9H specifically proliferated and produced gamma-interferon in response to recombinant protein and one individual  
30 peptide as well as the peptide pool. Following re-stimulation on targets loaded with the specific peptide, only 3A9H responded specifically to targets exposed to lysates of

fibroblasts infected adenovirus expressing full-length P703P. These results indicates that the line 3A9H can respond to antigenic peptide derived from protein synthesized in mammalian cells. The peptide to which the specific CD4 line responded correspond to amino acids 155-170 of P703P (SEQ ID NO: 943). The DNA sequence for this peptide  
5 is provided in SEQ ID NO: 942.

### EXAMPLE 11

#### EXPRESSION OF A BREAST TUMOR-DERIVED ANTIGEN IN PROSTATE

10

Isolation of the antigen B305D from breast tumor by differential display is described in US Patent Application No. 08/700,014, filed August 20, 1996. Several different splice forms of this antigen were isolated. The determined cDNA sequences for these splice forms are provided in SEQ ID NO: 366-375, with the predicted amino  
15 acid sequences corresponding to the sequences of SEQ ID NO: 292, 298 and 301-303 being provided in SEQ ID NO: 299-306, respectively. In further studies, a splice variant of the cDNA sequence of SEQ ID NO: 366 was isolated which was found to contain an additional guanine residue at position 884 (SEQ ID NO: 530), leading to a frameshift in the open reading frame. The determined DNA sequence of this ORF is  
20 provided in SEQ ID NO: 531. This frameshift generates a protein sequence (provided in SEQ ID NO: 532) of 293 amino acids that contains the C-terminal domain common to the other isoforms of B305D but that differs in the N-terminal region.

The expression levels of B305D in a variety of tumor and normal tissues were examined by real time PCR and by Northern analysis. The results indicated that  
25 B305D is highly expressed in breast tumor, prostate tumor, normal prostate and normal testes, with expression being low or undetectable in all other tissues examined (colon tumor, lung tumor, ovary tumor, and normal bone marrow, colon, kidney, liver, lung, ovary, skin, small intestine, stomach). Using real-time PCR on a panel of prostate tumors, expression of B305D in prostate tumors was shown to increase with increasing

Gleason grade, demonstrating that expression of B305D increases as prostate cancer progresses.

## EXAMPLE 12

### 5 GENERATION OF HUMAN CTL *IN VITRO* USING WHOLE GENE PRIMING AND STIMULATION TECHNIQUES WITH THE PROSTATE-SPECIFIC ANTIGEN P501S

Using *in vitro* whole-gene priming with P501S-vaccinia infected DC (see, for example, Yee et al, *The Journal of Immunology*, 157(9):4079-86, 1996),  
10 human CTL lines were derived that specifically recognize autologous fibroblasts transduced with P501S (also known as L1-12), as determined by interferon- $\gamma$  ELISPOT analysis as described above. Using a panel of HLA-mismatched B-LCL lines transduced with P501S, these CTL lines were shown to be likely restricted to HLAB class I allele. Specifically, dendritic cells (DC) were differentiated from monocyte  
15 cultures derived from PBMC of normal human donors by growing for five days in RPMI medium containing 10% human serum, 50 ng/ml human GM-CSF and 30 ng/ml human IL-4. Following culture, DC were infected overnight with recombinant P501S vaccinia virus at a multiplicity of infection (M.O.I) of five, and matured overnight by the addition of 3  $\mu$ g/ml CD40 ligand. Virus was inactivated by UV irradiation. CD8+  
20 T cells were isolated using a magnetic bead system, and priming cultures were initiated using standard culture techniques. Cultures were restimulated every 7-10 days using autologous primary fibroblasts retrovirally transduced with P501S and CD80. Following four stimulation cycles, CD8+ T cell lines were identified that specifically produced interferon- $\gamma$  when stimulated with P501S and CD80-transduced autologous  
25 fibroblasts. A panel of HLA-mismatched B-LCL lines transduced with P501S were generated to define the restriction allele of the response. By measuring interferon- $\gamma$  in an ELISPOT assay, the P501S specific response was shown to be likely restricted by HLA B alleles. These results demonstrate that a CD8+ CTL response to P501S can be elicited.

To identify the epitope(s) recognized, cDNA encoding P501S was fragmented by various restriction digests, and sub-cloned into the retroviral expression vector pBIB-KS. Retroviral supernatants were generated by transfection of the helper packaging line Phoenix-Ampho. Supernatants were then used to transduce  
5 Jurkat/A2Kb cells for CTL screening. CTL were screened in IFN-gamma ELISPOT assays against these A2Kb targets transduced with the "library" of P501S fragments. Initial positive fragments P501S/H3 and P501S/F2 were sequenced and found to encode amino acids 106-553 and amino acids 136-547, respectively, of SEQ ID NO: 113. A truncation of H3 was made to encode amino acid residues 106-351 of SEQ ID NO: 113,  
10 which was unable to stimulate the CTL, thus localizing the epitope to amino acid residues 351-547. Additional fragments encoding amino acids 1-472 (Fragment A) and amino acids 1-351 (Fragment B) were also constructed. Fragment A but not Fragment B stimulated the CTL thus localizing the epitope to amino acid residues 351-472. Overlapping 20-mer and 18-mer peptides representing this region were tested by pulsing  
15 Jurkat/A2Kb cells versus CTL in an IFN-gamma assay. Only peptides P501S-369(20) and P501S-369(18) stimulated the CTL. Nine-mer and 10-mer peptides representing this region were synthesized and similarly tested. Peptide P501S-370 (SEQ ID NO: 539) was the minimal 9-mer giving a strong response. Peptide P501S-376 (SEQ ID NO: 540) also gave a weak response, suggesting that it might represent a cross-reactive  
20 epitope.

In subsequent studies, the ability of primary human B cells transduced with P501S to prime MHC class I-restricted, P501S-specific, autologous CD8 T cells was examined. Primary B cells were derived from PBMC of a homozygous HLA-A2 donor by culture in CD40 ligand and IL-4, transduced at high frequency with  
25 recombinant P501S in the vector pBIB, and selected with blastocidin-S. For *in vitro* priming, purified CD8+ T cells were cultured with autologous CD40 ligand + IL-4 derived, P501S-transduced B cells in a 96-well microculture format. These CTL microcultures were re-stimulated with P501S-transduced B cells and then assayed for specificity. Following this initial screen, microcultures with significant signal above  
30 background were cloned on autologous EBV-transformed B cells (BLCL), also

transduced with P501S. Using IFN-gamma ELISPOT for detection, several of these CD8 T cell clones were found to be specific for P501S, as demonstrated by reactivity to BLCL/P501S but not BLCL transduced with control antigen. It was further demonstrated that the anti-P501S CD8 T cell specificity is HLA-A2-restricted. First, antibody blocking experiments with anti-HLA-A,B,C monoclonal antibody (W6.32), anti-HLA-B,C monoclonal antibody (B1.23.2) and a control monoclonal antibody showed that only the anti-HLA-A,B,C antibody blocked recognition of P501S-expressing autologous BLCL. Secondly, the anti-P501S CTL also recognized an HLA-A2 matched, heterologous BLCL transduced with P501S, but not the corresponding EGFP transduced control BLCL.

A naturally processed, CD8, class I-restricted peptide epitope of P501S was identified as follows. Dendritic Cells (DC) were isolated by Percol gradient followed by differential adherence, and cultured for 5 days in the presence of RPMI medium containing 1% human serum, 50ng/ml GM-CSF and 30ng/ml IL-4. Following culture, DC were infected for 24 hours with P501S-expressing adenovirus at an MOI of 10 and matured for an additional 24 hours by the addition of 2ug/ml CD40 ligand. CD8 cells were enriched for by the subtraction of CD4+, CD14+ and CD16+ populations from PBMC with magnetic beads. Priming cultures containing 10,000 P501S-expressing DC and 100,000 CD8+ T cells per well were set up in 96-well V-bottom plates with RPMI containing 10% human serum, 5ng/ml IL-12 and 10ng/ml IL-6. Cultures were stimulated every 7 days using autologous fibroblasts retrovirally transduced to express P501S and CD80, and were treated with IFN-gamma for 48-72 hours to upregulate MHC Class I expression. 10u/ml IL-2 was added at the time of stimulation and on days 2 and 5 following stimulation. Following 4 stimulation cycles, one P501S-specific CD8+ T cell line (referred to as 2A2) was identified that produced IFN-gamma in response to IFN-gamma-treated P501S/CD80 expressing autologous fibroblasts, but not in response to IFN-gamma-treated P703P/CD80 expressing autologous fibroblasts in a  $\gamma$ -IFN Elispot assay. Line 2A2 was cloned in 96-well plates with 0.5 cell/well or 2 cells/well in the presence of 75,000 PBMC/well, 10,000 B-LCL/well, 30ng/ml OKT3 and 50u/ml IL-2. Twelve clones were isolated that showed strong P501S specificity in response to transduced fibroblasts.

Fluorescence activated cell sorting (FACS) analysis was performed on P501S-specific clones using CD3-, CD4- and CD8-specific antibodies conjugated to PercP, FITC and PE respectively. Consistent with the use of CD8 enriched T cells in the priming cultures, P5401S-specific clones were determined to be CD3+, CD8+ and  
5 CD4-.

To identify the relevant P501S epitope recognized by P501S specific CTL, pools of 18-20 mer or 30-mer peptides that spanned the majority of the amino acid sequence of P501S were loaded onto autologous B-LCL and tested in  $\gamma$ -IFN Elispot assays for the ability to stimulate two P501S-specific CTL clones, referred to as 4E5  
10 and 4E7. One pool, composed of five 18-20 mer peptides that spanned amino acids 411-486 of P501S (SEQ ID NO: 113), was found to be recognized by both P501S-specific clones. To identify the specific 18-20 mer peptide recognized by the clones, each of the 18-20 mer peptides that comprised the positive pool were tested individually in  $\gamma$ -IFN Elispot assays for the ability to stimulate the two P501S-specific CTL clones, 4E5 and  
15 4E7. Both 4E5 and 4E7 specifically recognized one 20-mer peptide (SEQ ID NO: 853; cDNA sequence provided in SEQ ID NO: 854) that spanned amino acids 453-472 of P501S. Since the minimal epitope recognized by CD8+ T cells is almost always either a 9 or 10-mer peptide sequence, 10-mer peptides that spanned the entire sequence of SEQ ID NO: 853 were synthesized that differed by 1 amino acid. Each of these 10-mer  
20 peptides was tested for the ability to stimulate two P501S-specific clones, (referred to as 1D5 and 1E12). One 10-mer peptide (SEQ ID NO: 855; cDNA sequence provided in SEQ ID NO: 856) was identified that specifically stimulated the P501S-specific clones. This epitope spans amino acids 463-472 of P501S. This sequence defines a minimal 10-mer epitope from P501S that can be naturally processed and to which CTL responses  
25 can be identified in normal PBMC. Thus, this epitope is a candidate for use as a vaccine moiety, and as a therapeutic and/or diagnostic reagent for prostate cancer.

To identify the class I restriction element for the P501S-derived sequence of SEQ ID NO: 855, HLA blocking and mismatch analyses were performed. In  $\gamma$ -IFN Elispot assays, the specific response of clones 4A7 and 4E5 to P501S-transduced  
30 autologous fibroblasts was blocked by pre-incubation with 25ug/ml W6/32 (pan-Class I blocking antibody) and B1.23.2 (HLA-B/C blocking antibody). These results

demonstrate that the SEQ ID NO: 855-specific response is restricted to an HLA-B or HLA-C allele.

For the HLA mismatch analysis, autologous B-LCL (HLA-A1,A2,B8,B51, Cw1, Cw7) and heterologous B-LCL (HLA-A2,A3,B18,B51,Cw5,Cw14) that share the HLAB51 allele were pulsed for one hour with 20ug/ml of peptide of SEQ ID NO: 855, washed, and tested in  $\gamma$ -IFN Elispot assays for the ability to stimulate clones 4A7 and 4E5. Antibody blocking assays with the B1.23.2 (HLA-B/C blocking antibody) were also performed. SEQ ID NO: 855-specific response was detected using both the autologous (D326) and heterologous (D107) B-LCL, and furthermore the responses were blocked by pre-incubation with 25ug/ml of B1.23.2 HLA-B/C blocking antibody. Together these results demonstrate that the P501S-specific response to the peptide of SEQ ID NO: 855 is restricted to the HLA-B51 class I allele. Molecular cloning and sequence analysis of the HLA-B51 allele from D3326 revealed that the HLA-B51 subtype of D326 is HLA-B51011.

Based on the 10-mer P501S-derived epitope of SEQ ID NO: 855, two 9-mers with the sequences of SEQ ID NO: 857 and 858 were synthesized and tested in Elispot assays for the ability to stimulate two P501S-specific CTL clones derived from line 2A2. The 10-mer peptide of SEQ ID NO: 855, as well as the 9-mer peptide of SEQ ID NO: 858, but not the 9-mer peptide of SEQ ID NO: 857, were capable of stimulating the P501S-specific CTL to produce IFN-gamma. These results demonstrate that the peptide of SEQ ID NO: 858 is a 9-mer P501S-derived epitope recognized by P501S-specific CTL. The DNA sequence encoding the epitope of SEQ ID NO: 858 is provided in SEQ ID NO: 859.

To identify the class I restricting allele for the P501S-derived peptide of SEQ ID NO: 855 and 858 specific response, each of the HLA B and C alleles were cloned from the donor used in the *in vitro* priming experiment. Sequence analysis indicated that the relevant alleles were HLA-B8, HLA-B51, HLA-Cw01 and HLA-Cw07. Each of these alleles were subcloned into an expression vector and co-transfected together with the P501S gene into VA-13 cells. Transfected VA-13 cells were then tested for the ability to specifically stimulate the P501S-specific CTL in ELISPOT assays. VA-13 cells transfected with P501S and HLA-B51 were capable of

stimulating the P501S-specific CTL to secrete gamma-IFN. VA-13 cells transfected with HLA-B51 alone or P501S + the other HLA-alleles were not capable of stimulating the P501S-specific CTL. These results demonstrate that the restricting allele for the P501S-specific response is the HLAB51 allele. Sequence analysis revealed that the  
5 subtype of the relevant restricting allele is HLA-B51011.

To determine if the P501S-specific CTL could recognize prostate tumor cells that express P501S, the P501S-positive lines LnCAP and CRL2422 (both expressing "moderate" amounts of P501S mRNA and protein), and PC-3 (expressing low amounts of P501S mRNA and protein), plus the P501S-negative cell line DU-145  
10 were retrovirally transduced with the HLA-B51011 allele that was cloned from the donor used to generate the P501S-specific CTL. HLA-B51011- or EGFP-transduced and selected tumor cells were treated with gamma-interferon and androgen (to upregulate stimulatory functions and P501S, respectively) and used in gamma-interferon Elispot assays with the P501S-specific CTL clones 4E5 and 4E7. Untreated  
15 cells were used as a control.

Both 4E5 and 4E7 efficiently and specifically recognized LnCAP and CRL2422 cells that were transduced with the HLA-B51011 allele, but not the same cell lines transduced with EGFP. Additionally, both CTL clones specifically recognized PC-3 cells transduced with HLA-B51011, but not the P501S-negative tumor cell line  
20 DU-145. Treatment with gamma-interferon or androgen did not enhance the ability of CTL to recognize tumor cells. These results demonstrate that P501S-specific CTL, generated by *in vitro* whole gene priming, specifically and efficiently recognize prostate tumor cell lines that express P501S.

A naturally processed CD4 epitope of P501S was identified as follows.

25 CD4 cells specific for P501S were prepared as described above. A series of 16 overlapping peptides were synthesized that spanned approximately 50% of the amino terminal portion of the P501S gene (amino acids 1- 325 of SEQ ID NO: 113). For priming, peptides were combined into pools of 4 peptides, pulsed at 4 µg/ml onto dendritic cells (DC) for 24 hours, with TNF-alpha. DC were then washed and mixed  
30 with negatively selected CD4+ T cells in 96 well U-bottom plates. Cultures were re-stimulated weekly on fresh DC loaded with peptide pools. Following a total of 4



stimulation cycles, cells were rested for an additional week and tested for specificity to APC pulsed with peptide pools using  $\gamma$ -IFN ELISA and proliferation assays. For these assays, adherent monocytes loaded with either the relevant peptide pool at 4 $\mu$ g/ml or an irrelevant peptide at  $\mu$ g/ml were used as APC. T cell lines that demonstrated either  
5 specific cytokine secretion or proliferation were then tested for recognition of individual peptides that were present in the pool. T cell lines could be identified from pools A and B that recognized individual peptides from these pools.

From pool A, lines AD9 and AE10 specifically recognized peptide 1 (SEQ ID NO: 862), and line AF5 recognized peptide 39 (SEQ ID NO: 861). From pool  
10 B, line BC6 could be identified that recognized peptide 58 (SEQ ID NO: 860). Each of these lines were stimulated on the specific peptide and tested for specific recognition of the peptide in a titration assay as well as cell lysates generated by infection of HEK 293 cells with adenovirus expressing either P501S or an irrelevant antigen. For these assays, APC-adherent monocytes were pulsed with either 10, 1, or 0.1  $\mu$ g/ml individual P501S  
15 peptides, and DC were pulsed overnight with a 1:5 dilution of adenovirally infected cell lysates. Lines AD9, AE10 and AF5 retained significant recognition of the relevant P501S-derived peptides even at 0.1 mg/ml. Furthermore, line AD9 demonstrated significant (8.1 fold stimulation index) specific activity for lysates from adenovirus-P501S infected cells. These results demonstrate that high affinity CD4 T cell lines can  
20 be generated toward P501S-derived epitopes, and that at least a subset of these T cells specific for the P501S derived sequence of SEQ ID NO: 862 are specific for an epitope that is naturally processed by human cells. The DNA sequences encoding the amino acid sequences of SEQ ID NO: 860-862 are provided in SEQ ID NO: 863-865, respectively.

25 To further characterize the P501S-specific activity of AD9, the line was cloned using anti-CD3. Three clones, referred to as 1A1, 1A9 and 1F5, were identified that were specific for the P501S-1 peptide (SEQ ID NO: 862). To determine the HLA restriction allele for the P501S-specific response, each of these clones was tested in class II antibody blocking and HLA mismatch assays using proliferation and gamma-interferon assays. In antibody blocking assays and measuring gamma-interferon  
30 production using ELISA assays, the ability of all three clones to recognize peptide

pulsed APC was specifically blocked by co-incubation with either a pan-class II blocking antibody or a HLA-DR blocking antibody, but not with a HLA-DQ or an irrelevant antibody. Proliferation assays performed simultaneously with the same cells confirmed these results. These data indicate that the P501S-specific response of the clones is restricted by an HLA-DR allele. Further studies demonstrated that the restricting allele for the P501S-specific response is HLA-DRB1501.

### EXAMPLE 13

#### IDENTIFICATION OF PROSTATE-SPECIFIC ANTIGENS

#### BY MICROARRAY ANALYSIS

This Example describes the isolation of certain prostate-specific polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library as described above was screened using microarray analysis to identify clones that display at least a three fold over-expression in prostate tumor and/or normal prostate tissue, as compared to non-prostate normal tissues (not including testis). 372 clones were identified, and 319 were successfully sequenced. Table I presents a summary of these clones, which are shown in SEQ ID NOs:385-400. Of these sequences SEQ ID NOs:386, 389, 390 and 392 correspond to novel genes, and SEQ ID NOs: 393 and 396 correspond to previously identified sequences. The others (SEQ ID NOs:385, 387, 388, 391, 394, 395 and 397-400) correspond to known sequences, as shown in Table I.

Table ISummary of Prostate Tumor Antigens

Known Genes	Previously Identified Genes	Novel Genes
T-cell gamma chain	P504S	23379 (SEQ ID NO:389)
Kallikrein	P1000C	23399 (SEQ ID NO:392)
Vector	P501S	23320 (SEQ ID NO:386)
CGI-82 protein mRNA (23319; SEQ ID NO:385)	P503S	23381 (SEQ ID NO:390)
PSA	P510S	
Ald. 6 Dehyd.	P784P	
L-iditol-2 dehydrogenase (23376; SEQ ID NO:388)	P502S	
Ets transcription factor PDEF (22672; SEQ ID NO:398)	P706P	
hTGR (22678; SEQ ID NO:399)	19142.2, bangur.seq (22621; SEQ ID NO:396)	
KIAA0295(22685; SEQ ID NO:400)	5566.1 Wang (23404; SEQ ID NO:393)	
Prostatic Acid Phosphatase(22655; SEQ ID NO:397)	P712P	
transglutaminase (22611; SEQ ID NO:395)	P778P	
HDLBP (23508; SEQ ID NO:394)		
CGI-69 Protein(23367; SEQ ID NO:387)		
KIAA0122(23383; SEQ ID NO:391)		
TEEG		

CGI-82 showed 4.06 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 43% of prostate tumors, 25% normal prostate, not detected in other normal tissues tested. L-Iditol-2 dehydrogenase showed 4.94 fold over-expression in prostate tissues as compared to  
5 other normal tissues tested. It was over-expressed in 90% of prostate tumors, 100% of normal prostate, and not detected in other normal tissues tested. Ets transcription factor PDEF showed 5.55 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 47% prostate tumors, 25% normal prostate and not detected in other normal tissues tested. hTGR1 showed 9.11 fold over-expression in  
10 prostate tissues as compared to other normal tissues tested. It was over-expressed in 63% of prostate tumors and is not detected in normal tissues tested including normal prostate. KIAA0295 showed 5.59 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 47% of prostate tumors, low to undetectable in normal tissues tested including normal prostate tissues. Prostatic acid  
15 phosphatase showed 9.14 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 67% of prostate tumors, 50% of normal prostate, and not detected in other normal tissues tested. Transglutaminase showed 14.84 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 30% of prostate tumors, 50% of normal prostate, and is  
20 not detected in other normal tissues tested. High density lipoprotein binding protein (HDLBP) showed 28.06 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 97% of prostate tumors, 75% of normal prostate, and is undetectable in all other normal tissues tested. CGI-69 showed 3.56 fold over-expression in prostate tissues as compared to other normal tissues tested. It is  
25 a low abundant gene, detected in more than 90% of prostate tumors, and in 75% normal prostate tissues. The expression of this gene in normal tissues was very low. KIAA0122 showed 4.24 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 57% of prostate tumors, it was undetectable in all normal tissues tested including normal prostate tissues. 19142.2  
30 bangur showed 23.25 fold over-expression in prostate tissues as compared to other

normal tissues tested. It was over-expressed in 97% of prostate tumors and 100% of normal prostate. It was undetectable in other normal tissues tested. 5566.1 Wang showed 3.31 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 97% of prostate tumors, 75% normal prostate and was also over-expressed in normal bone marrow, pancreas, and activated PBMC. Novel clone 23379 (also referred to as P553S) showed 4.86 fold over-expression in prostate tissues as compared to other normal tissues tested. It was detectable in 97% of prostate tumors and 75% normal prostate and is undetectable in all other normal tissues tested. Novel clone 23399 showed 4.09 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 27% of prostate tumors and was undetectable in all normal tissues tested including normal prostate tissues. Novel clone 23320 showed 3.15 fold over-expression in prostate tissues as compared to other normal tissues tested. It was detectable in all prostate tumors and 50% of normal prostate tissues. It was also expressed in normal colon and trachea. Other normal tissues do not express this gene at high level.

Subsequent full-length cloning studies on P553S, using standard techniques, revealed that this clone is an incomplete spliced form of P501S. The determined cDNA sequences for four splice variants of P553S are provided in SEQ ID NO: 702-705. An amino acid sequence encoded by SEQ ID NO: 705 is provided in SEQ ID NO: 706. The cDNA sequence of SEQ ID NO: 702 was found to contain two open reading frames (ORFs). The amino acid sequences encoded by these two ORFs are provided in SEQ ID NO: 707 and 708.

#### EXAMPLE 14

#### IDENTIFICATION OF PROSTATE-SPECIFIC ANTIGENS BY ELECTRONIC SUBTRACTION

This Example describes the use of an electronic subtraction technique to identify prostate-specific antigens.

Potential prostate-specific genes present in the GenBank human EST database were identified by electronic subtraction (similar to that described by Vasmatizis et al., *Proc. Natl. Acad. Sci. USA* 95:300-304, 1998). The sequences of EST clones (43,482) derived from various prostate libraries were obtained from the GenBank  
5 public human EST database. Each prostate EST sequence was used as a query sequence in a BLASTN (National Center for Biotechnology Information) search against the human EST database. All matches considered identical (length of matching sequence >100 base pairs, density of identical matches over this region > 70%) were grouped (aligned) together in a cluster. Clusters containing more than 200 ESTs were discarded  
10 since they probably represented repetitive elements or highly expressed genes such as those for ribosomal proteins. If two or more clusters shared common ESTs, those clusters were grouped together into a "supercluster," resulting in 4,345 prostate superclusters.

Records for the 479 human cDNA libraries represented in the GenBank  
15 release were downloaded to create a database of these cDNA library records. These 479 cDNA libraries were grouped into three groups: Plus (normal prostate and prostate tumor libraries, and breast cell line libraries, in which expression was desired), Minus (libraries from other normal adult tissues, in which expression was not desirable), and Other (libraries from fetal tissue, infant tissue, tissues found only in women, non-  
20 prostate tumors and cell lines other than prostate cell lines, in which expression was considered to be irrelevant). A summary of these library groups is presented in Table II.

Table II  
Prostate cDNA Libraries and ESTs

Library	# of Libraries	# of ESTs
Plus	25	43,482
Normal	11	18,875
Tumor	11	21,769
Cell lines	3	2,838
Minus	166	
Other	287	

5            Each supercluster was analyzed in terms of the ESTs within the supercluster. The tissue source of each EST clone was noted and used to classify the superclusters into four groups: Type 1- EST clones found in the Plus group libraries only; no expression detected in Minus or Other group libraries; Type 2- EST clones derived from the Plus and Other group libraries only; no expression detected in the

10 Minus group; Type 3- EST clones derived from the Plus, Minus and Other group libraries, but the number of ESTs derived from the Plus group is higher than in either the Minus or Other groups; and Type 4- EST clones derived from Plus, Minus and Other group libraries, but the number derived from the Plus group is higher than the number derived from the Minus group. This analysis identified 4,345 breast clusters

15 (see Table III). From these clusters, 3,172 EST clones were ordered from Research Genetics, Inc., and were received as frozen glycerol stocks in 96-well plates.

Table III  
Prostate Cluster Summary

Type	# of Superclusters	# of ESTs Ordered
1	688	677
2	2899	2484
3	85	11
4	673	0
Total	4345	3172

5           The EST clone inserts were PCR-amplified using amino-linked PCR primers for Synteni microarray analysis. When more than one PCR product was obtained for a particular clone, that PCR product was not used for expression analysis. In total, 2,528 clones from the electronic subtraction method were analyzed by microarray analysis to identify electronic subtraction breast clones that had high levels  
10 of tumor vs. normal tissue mRNA. Such screens were performed using a Synteni (Palo Alto, CA) microarray, according to the manufacturer's instructions (and essentially as described by Schena et al., *Proc. Natl. Acad. Sci. USA* 93:10614-10619, 1996 and Heller et al., *Proc. Natl. Acad. Sci. USA* 94:2150-2155, 1997). Within these analyses, the clones were arrayed on the chip, which was then probed with fluorescent probes  
15 generated from normal and tumor prostate cDNA, as well as various other normal tissues. The slides were scanned and the fluorescence intensity was measured.

          Clones with an expression ratio greater than 3 (*i.e.*, the level in prostate tumor and normal prostate mRNA was at least three times the level in other normal tissue mRNA) were identified as prostate tumor-specific sequences (Table IV). The  
20 sequences of these clones are provided in SEQ ID NO: 401-453, with certain novel sequences shown in SEQ ID NO: 407, 413, 416-419, 422, 426, 427 and 450.



Table IV

Prostate-tumor Specific Clones

SEQ ID NO.	Sequence Designation	Comments
401	22545	previously identified P1000C
402	22547	previously identified P704P
403	22548	known
404	22550	known
405	22551	PSA
406	22552	prostate secretory protein 94
407	22553	novel
408	22558	previously identified P509S
409	22562	glandular kallikrein
410	22565	previously identified P1000C
411	22567	PAP
412	22568	B1006C (breast tumor antigen)
413	22570	novel
414	22571	PSA
415	22572	previously identified P706P
416	22573	novel
417	22574	novel
418	22575	novel
419	22580	novel
420	22581	PAP
421	22582	prostatic secretory protein 94
422	22583	novel
423	22584	prostatic secretory protein 94
424	22585	prostatic secretory protein 94
425	22586	known
426	22587	novel
427	22588	novel
428	22589	PAP
429	22590	known
430	22591	PSA
431	22592	known
432	22593	Previously identified P777P
433	22594	T cell receptor gamma chain
434	22595	Previously identified P705P
435	22596	Previously identified P707P
436	22847	PAP
437	22848	known
438	22849	prostatic secretory protein 57

439	22851	PAP
440	22852	PAP
441	22853	PAP
442	22854	previously identified P509S
443	22855	previously identified P705P
444	22856	previously identified P774P
445	22857	PSA
446	23601	previously identified P777P
447	23602	PSA
448	23605	PSA
449	23606	PSA
450	23612	novel
451	23614	PSA
452	23618	previously identified P1000C
453	23622	previously identified P705P

Further studies on the clone of SEQ ID NO: 407 (also referred to as P1020C) led to the isolation of an extended cDNA sequence provided in SEQ ID NO: 591. This extended cDNA sequence was found to contain an open reading frame that  
5 encodes the predicted amino acid sequence of SEQ ID NO: 592. The P1020C cDNA and amino acid sequences were found to show some similarity to the human endogenous retroviral HERV-K pol gene and protein.

#### EXAMPLE 15

##### 10 FURTHER IDENTIFICATION OF PROSTATE-SPECIFIC ANTIGENS BY MICROARRAY ANALYSIS

This Example describes the isolation of additional prostate-specific polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library as described above  
15 was screened using microarray analysis to identify clones that display at least a three fold over-expression in prostate tumor and/or normal prostate tissue, as compared to non-prostate normal tissues (not including testis). 142 clones were identified and sequenced. Certain of these clones are shown in SEQ ID NO: 454-467. Of these sequences, SEQ ID NO: 459-460 represent novel genes. The others (SEQ ID NO: 454-  
20 458 and 461-467) correspond to known sequences. Comparison of the determined

cDNA sequence of SEQ ID NO: 461 with sequences in the Genbank database using the BLAST program revealed homology to the previously identified transmembrane protease serine 2 (TMPRSS2). The full-length cDNA sequence for this clone is provided in SEQ ID NO: 894, with the corresponding amino acid sequence being  
5 provided in SEQ ID NO: 895. The cDNA sequence encoding the first 209 amino acids of TMPRSS2 is provided in SEQ ID NO: 896, with the first 209 amino acids being provided in SEQ ID NO: 897.

The sequence of SEQ ID NO: 462 (referred to as P835P) was found to correspond to the previously identified clone FLJ13518 (Accession AK023643; SEQ ID  
10 NO: 917), which had no associated open reading frame (ORF). This clone was used to search the Geneseq DNA database and matched a clone previously identified as a G protein-coupled receptor protein (DNA Geneseq Accession A09351; amino acid Geneseq Accession Y92365), that is characterized by the presence of seven transmembrane domains. The sequences of fragments between these domains are  
15 provided in SEQ ID NO: 921-928, with SEQ ID NO: 921, 923, 925 and 927 representing extracellular domains and SEQ ID NO: 922, 924, 926 and 928 representing intracellular domains. SEQ ID NO: 921-928 represent amino acids 1-28, 53-61, 83-103, 124-143, 165-201, 226-238, 263-272 and 297-381, respectively, of P835P. The full-length cDNA sequence for P835P is provided in SEQ ID NO: 916. The cDNA  
20 sequence of the open reading frame for P835P, including stop codon, is provided in SEQ ID NO: 918, with the open reading frame without stop codon being provided in SEQ ID NO: 919 and the corresponding amino acid sequence being provided in SEQ ID NO: 920.

25

## EXAMPLE 16

## FURTHER CHARACTERIZATION OF PROSTATE-SPECIFIC ANTIGEN P710P

This Example describes the full length cloning of P710P.

The prostate cDNA library described above was screened with the P710P  
30 fragment described above. One million colonies were plated on LB/Ampicillin plates.

Nylon membrane filters were used to lift these colonies, and the cDNAs picked up by these filters were then denatured and cross-linked to the filters by UV light. The P710P fragment was radiolabeled and used to hybridize with the filters. Positive cDNA clones were selected and their cDNAs recovered and sequenced by an automatic Perkin Elmer/Applied Biosystems Division Sequencer. Four sequences were obtained, and are presented in SEQ ID NO: 468-471. These sequences appear to represent different splice variants of the P710P gene. Subsequent comparison of the cDNA sequences of P710P with those in Genbank revealed homology to the DD3 gene (Genbank accession numbers AF103907 & AF103908). The cDNA sequence of DD3 is provided in SEQ ID NO: 690.

#### EXAMPLE 17

##### PROTEIN EXPRESSION OF PROSTATE-SPECIFIC ANTIGENS

This example describes the expression and purification of prostate-specific antigens in *E. coli*, baculovirus and mammalian cells.

##### a) Expression of P501S in *E. coli*

Expression of the full-length form of P501S was attempted by first cloning P501S without the leader sequence (amino acids 36-553 of SEQ ID NO: 113) downstream of the first 30 amino acids of the *M. tuberculosis* antigen Ra12 (SEQ ID NO: 484) in pET17b. Specifically, P501S DNA was used to perform PCR using the primers AW025 (SEQ ID NO: 485) and AW003 (SEQ ID NO: 486). AW025 is a sense cloning primer that contains a HindIII site. AW003 is an antisense cloning primer that contains an EcoRI site. DNA amplification was performed using 5 µl 10X Pfu buffer, 1 µl 20 mM dNTPs, 1 µl each of the PCR primers at 10 µM concentration, 40 µl water, 1 µl Pfu DNA polymerase (Stratagene, La Jolla, CA) and 1 µl DNA at 100 ng/µl. Denaturation at 95°C was performed for 30 sec, followed by 10 cycles of 95°C for 30 sec, 60°C for 1 min and by 72°C for 3 min. 20 cycles of 95°C for 30 sec, 65°C for 1 min and by 72°C for 3 min, and lastly by 1 cycle of 72°C for 10 min. The PCR product was

cloned to Ra12m/pET17b using HindIII and EcoRI. The sequence of the resulting fusion construct (referred to as Ra12-P501S-F) was confirmed by DNA sequencing.

The fusion construct was transformed into BL21(DE3)pLysE, pLysS and CodonPlus *E. coli* (Stratagene) and grown overnight in LB broth with kanamycin. The  
5 resulting culture was induced with IPTG. Protein was transferred to PVDF membrane and blocked with 5% non-fat milk (in PBS-Tween buffer), washed three times and incubated with mouse anti-His tag antibody (Clontech) for 1 hour. The membrane was washed 3 times and probed with HRP-Protein A (Zymed) for 30 min. Finally, the membrane was washed 3 times and developed with ECL (Amersham). No expression  
10 was detected by Western blot. Similarly, no expression was detected by Western blot when the Ra12-P501S-F fusion was used for expression in BL21CodonPlus by CE6 phage (Invitrogen).

An N-terminal fragment of P501S (amino acids 36-325 of SEQ ID NO: 113) was cloned down-stream of the first 30 amino acids of the *M. tuberculosis* antigen Ra12 in pET17b as follows. P501S DNA was used to perform PCR using the primers  
15 AW025 (SEQ ID NO: 485) and AW027 (SEQ ID NO: 487). AW027 is an antisense cloning primer that contains an EcoRI site and a stop codon. DNA amplification was performed essentially as described above. The resulting PCR product was cloned to Ra12 in pET17b at the HindIII and EcoRI sites. The fusion construct (referred to as  
20 Ra12-P501S-N) was confirmed by DNA sequencing.

The Ra12-P501S-N fusion construct was used for expression in BL21(DE3)pLysE, pLysS and CodonPlus, essentially as described above. Using Western blot analysis, protein bands were observed at the expected molecular weight of 36 kDa. Some high molecular weight bands were also observed, probably due to  
25 aggregation of the recombinant protein. No expression was detected by Western blot when the Ra12-P501S-F fusion was used for expression in BL21CodonPlus by CE6 phage.

A fusion construct comprising a C-terminal portion of P501S (amino acids 257-553 of SEQ ID NO: 113) located down-stream of the first 30 amino acids of the *M. tuberculosis* antigen Ra12 (SEQ ID NO: 484) was prepared as follows. P501S  
30

DNA was used to perform PCR using the primers AW026 (SEQ ID NO: 488) and AW003 (SEQ ID NO: 486). AW026 is a sense cloning primer that contains a HindIII site. DNA amplification was performed essentially as described above. The resulting PCR product was cloned to Ra12 in pET17b at the HindIII and EcoRI sites. The  
5 sequence for the fusion construct (referred to as Ra12-P501S-C) was confirmed.

The Ra12-P501S-C fusion construct was used for expression in BL21(DE3)pLysE, pLysS and CodonPlus, as described above. A small amount of protein was detected by Western blot, with some molecular weight aggregates also being observed. Expression was also detected by Western blot when the Ra12-P501S-C  
10 fusion was used for expression in BL21CodonPlus induced by CE6 phage.

A fusion construct comprising a fragment of P501S (amino acids 36-298 of SEQ ID NO: 113) located down-stream of the *M. tuberculosis* antigen Ra12 (SEQ ID NO: 848) was prepared as follows. P501S DNA was used to perform PCR using the primers AW042 (SEQ ID NO: 849) and AW053 (SEQ ID NO: 850). AW042 is a sense  
15 cloning primer that contains a EcoRI site. AW053 is an antisense primer with stop and Xho I sites. DNA amplification was performed essentially as described above. The resulting PCR product was cloned to Ra12 in pET17b at the EcoRI and Xho I sites. The resulting fusion construct (referred to as Ra12-P501S-E2) was expressed in B834 (DE3) pLys S *E. coli* host cells in TB media for 2 h at room temperature. Expressed protein  
20 was purified by washing the inclusion bodies and running on a Ni-NTA column. The purified protein stayed soluble in buffer containing 20 mM Tris-HCl (pH 8), 100 mM NaCl, 10 mM  $\beta$ -Me and 5% glycerol. The determined cDNA and amino acid sequences for the expressed fusion protein are provided in SEQ ID NO: 851 and 852, respectfully.

25 b) Expression of P501S in Baculovirus

The Bac-to-Bac baculovirus expression system (BRL Life Technologies, Inc.) was used to express P501S protein in insect cells. Full-length P501S (SEQ ID NO: 113) was amplified by PCR and cloned into the XbaI site of the donor plasmid pFastBacI. The recombinant bacmid and baculovirus were prepared according to the

manufacturer's instructions. The recombinant baculovirus was amplified in Sf9 cells and the high titer viral stocks were utilized to infect High Five cells (Invitrogen) to make the recombinant protein. The identity of the full-length protein was confirmed by N-terminal sequencing of the recombinant protein and by Western blot analysis (Figure 7). Specifically, 0.6 million High Five cells in 6-well plates were infected with either the unrelated control virus BV/ECD\_PD (lane 2), with recombinant baculovirus for P501S at different amounts or MOIs (lanes 4-8), or were uninfected (lane 3). Cell lysates were run on SDS-PAGE under reducing conditions and analyzed by Western blot with the anti-P501S monoclonal antibody P501S-10E3-G4D3 (prepared as described below). Lane 1 is the biotinylated protein molecular weight marker (BioLabs).

The localization of recombinant P501S in the insect cells was investigated as follows. The insect cells overexpressing P501S were fractionated into fractions of nucleus, mitochondria, membrane and cytosol. Equal amounts of protein from each fraction were analyzed by Western blot with a monoclonal antibody against P501S. Due to the scheme of fractionation, both nucleus and mitochondria fractions contain some plasma membrane components. However, the membrane fraction is basically free from mitochondria and nucleus. P501S was found to be present in all fractions that contain the membrane component, suggesting that P501S may be associated with plasma membrane of the insect cells expressing the recombinant protein.

#### c) Expression of P501S in mammalian cells

Full-length P501S (553 amino acids; SEQ ID NO: 113) was cloned into various mammalian expression vectors, including pCEP4 (Invitrogen), pVR1012 (Vical, San Diego, CA) and a modified form of the retroviral vector pBMN, referred to as pBIB. Transfection of P501S/pCEP4 and P501S/pVR1012 into HEK293 fibroblasts was carried out using the Fugene transfection reagent (Boehringer Mannheim). Briefly, 2 ul of Fugene reagent was diluted into 100 ul of serum-free media and incubated at room temperature for 5-10 min. This mixture was added to 1 ug of P501S plasmid DNA, mixed briefly and incubated for 30 minutes at room temperature. The

Fugene/DNA mixture was added to cells and incubated for 24-48 hours. Expression of recombinant P501S in transfected HEK293 fibroblasts was detected by means of Western blot employing a monoclonal antibody to P501S.

Transfection of p501S/pCEP4 into CHO-K cells (American Type Culture Collection, Rockville, MD) was carried out using GenePorter transfection reagent (Gene Therapy Systems, San Diego, CA). Briefly, 15  $\mu$ l of GenePorter was diluted in 500  $\mu$ l of serum-free media and incubated at room temperature for 10 min. The GenePorter/media mixture was added to 2  $\mu$ g of plasmid DNA that was diluted in 500  $\mu$ l of serum-free media, mixed briefly and incubated for 30 min at room temperature. CHO-K cells were rinsed in PBS to remove serum proteins, and the GenePorter/DNA mix was added and incubated for 5 hours. The transfected cells were then fed an equal volume of 2x media and incubated for 24-48 hours.

FACS analysis of P501S transiently infected CHO-K cells, demonstrated surface expression of P501S. Expression was detected using rabbit polyclonal antisera raised against a P501S peptide, as described below. Flow cytometric analysis was performed using a FaCScan (Becton Dickinson), and the data were analyzed using the Cell Quest program.

d) Expression of P703P in Baculovirus

The cDNA for full-length P703P-DE5 (SEQ ID NO: 326), together with several flanking restriction sites, was obtained by digesting the plasmid pCDNA703 with restriction endonucleases Xba I and Hind III. The resulting restriction fragment (approx. 800 base pairs) was ligated into the transfer plasmid pFastBacI which was digested with the same restriction enzymes. The sequence of the insert was confirmed by DNA sequencing. The recombinant transfer plasmid pFBP703 was used to make recombinant bacmid DNA and baculovirus using the Bac-To-Bac Baculovirus expression system (BRL Life Technologies). High Five cells were infected with the recombinant virus BVP703, as described above, to obtain recombinant P703P protein:



e) Expression of P788P in *E. Coli*

A truncated, N-terminal portion, of P788P (residues 1-644 of SEQ ID NO: 777; referred to as P788P-N) fused with a C-terminal 6xHis Tag was expressed in *E. coli* as follows. P788P cDNA was amplified using the primers AW080 and AW081 (SEQ ID NO: 815 and 816). AW080 is a sense cloning primer with an NdeI site. AW081 is an antisense cloning primer with a XhoI site. The PCR-amplified P788P, as well as the vector pCRX1, were digested with NdeI and XhoI. Vector and insert were ligated and transformed into NovaBlue cells. Colonies were randomly screened for insert and then sequenced. P788P-N clone #6 was confirmed to be identical to the designed construct. The expression construct P788P-N #6/pCRX1 was transformed into *E. coli* BL21 CodonPlus-RIL competent cells. After induction, most of the cells grew well, achieving OD600 of greater than 2.0 after 3 hr. Coomassie stained SDS-PAGE showed an over-expressed band at about 75 kD. Western blot analysis using a 6xHisTag antibody confirmed the band was P788P-N. The determined cDNA sequence for P788P-N is provided in SEQ ID NO: 817, with the corresponding amino acid sequence being provided in SEQ ID NO: 818.

f) Expression of P510S in *E. coli*

The P510S protein has 9 potential transmembrane domains and is predicted to be located at the plasma membrane. The C-terminal protein of this protein, as well as the predicted third extracellular domain of P510S were expressed in *E. coli* as follows.

The expression construct referred to as Ra12-P501S-C was designed to have a 6 HisTag at the N-terminal end, followed by the *M. tuberculosis* antigen Ra12 (SEQ ID NO: 819) and then the C-terminal portion of P510S (amino residues 1176-1261 of SEQ ID NO: 538). Full-length P510S was used to amplify the P510S-C fragment by PCR using the primers AW056 and AW057 (SEQ ID NO: 820 and 821, respectively). AW056 is a sense cloning primer with an EcoRI site. AW057 is an antisense primer with stop and XhoI sites. The amplified P501S fragment and Ra12/pCRX1 were digested with EcoRI and XhoI and then purified. The insert and

vector were ligated together and transformed into NovaBlue. Colonies were randomly screened for insert and sequences. For protein expression, the expression construct was transformed into *E. coli* BL21 (DE3) CodonPlus-RIL competent cells. A mini-induction screen was performed to optimize the expression conditions. After induction  
5 the cells grew well, achieving OD 600 nm greater than 2.0 after 3 hours. Coomassie stain SDS-PAGE showed a highly over-expressed band at approx. 30 kD. Though this is higher than the expected molecular weight, western blot analysis was positive, showing this band to be the His tag-containing protein. The optimized culture conditions are as follows. Dilute overnight culture/daytime culture (LB + kanamycin +  
10 chloramphenicol) into 2xYT (with kanamycin and chloramphenicol) at a ratio of 25 ml culture to 1 liter 2xYT. Allow to grow at 37 °C until OD600 = 0.6. Take an aliquot out as T0 sample. Add 1 mM IPTG and allow to grow at 30 °C for 3 hours. Take out a T3 sample, spin down cells and store at -80 °C. The determined cDNA and amino acid sequences for the Ra12-P510S-C construct are provided in SEQ ID NO: 822 and 825,  
15 respectively.

The expression construct P510S-C was designed to have a 5' added start codon and a glycine (GGA) codon and then the P510S C terminal fragment followed by the in frame 6x histidine tag and stop codon from the pET28b vector. The cloning strategy is similar to that used for Ra12-P510S-C, except that the PCR primers  
20 employed were those shown in SEQ ID NO: 828 and 829, respectively and the NcoI/XhoI cut in pET28b was used. The primer of SEQ ID NO: 828 created a 5' NcoI site and added a start codon. The antisense primer of SEQ ID NO: 829 creates a XhoI site on P510S C terminal fragment. Clones were confirmed by sequencing. For protein expression, the expression construct was transformed into *E. coli* BL21 (DE3)  
25 CodonPlus-RIL competent cells. An OD600 of greater than 2.0 was obtained 30 hours after induction. Coomassie stained SDS-PAGE showed an over-expressed band at about 11 kD. Western blot analysis confirmed that the band was P510S-C, as did N-terminal protein sequencing. The optimized culture conditions are as follows: dilute overnight culture/daytime culture (LB + kanamycin + chloramphenicol) into 2x YT (+  
30 kanamycin and chloramphenicol) at a ratio of 25 mL culture to 1 liter 2x YT, and allow

to grow at 37 °C until an OD 600 of about 0.5 is reached. Take out an aliquot as T0 sample. Add 1 mM IPTG and allow to grow at 30 °C for 3 hours. Spin down the cells and store at -80 °C until purification. The determined cDNA and amino acid sequences for the P510S-C construct are shown in SEQ ID NO: 823 and 826, respectively.

5           The predicted third extracellular domain of P510S (P510S-E3; residues 328-676 of SEQ ID NO: 538) was expressed in *E. coli* as follows. The P510S fragment was amplified by PCR using the primers shown in SEQ ID NO: 830 and 831. The primer of SEQ ID NO: 830 is a sense primer with an NdeI site for use in ligating into pPDM. The primer of SEQ ID NO: 831 is an antisense primer with an added XhoI site  
10 for use in ligating into pPDM. The resulting fragment was cloned to pPDM at the NdeI and XhoI sites. Clones were confirmed by sequencing. For protein expression, the clone was transformed into *E. coli* BL21 (DE3) CodonPlus-RIL competent cells. After induction, an OD600 of greater than 2.0 was achieved after 3 hours. Coomassie stained SDS-PAGE showed an over-expressed band at about 39 kD, and N-terminal sequencing  
15 confirmed the N-terminal to be that of P510S-E3. Optimized culture conditions are as follows: dilute overnight culture/daytime culture (LB + kanamycin + chloramphenicol) into 2x YT (kanamycin and chloramphenicol) at a ratio of 25 ml culture to 1 liter 2x YT. Allow to grow at 37 °C until OD 600 equals 0.6. Take out an aliquot as T0 sample. Add 1 mM IPTG and allow to grow at 30 °C for 3 hours. Take out a T3  
20 sample, spin down the cells and store at -80 °C until purification. The determined cDNA and amino acid sequences for the P501S-E3 construct are provided in SEQ ID NO: 824 and 827, respectively.

g) Expression of P775S in *E. Coli*

25           The antigen P775P contains multiple open reading frames (ORF). The third ORF, encoding the protein of SEQ ID NO: 483, has the best motif score. An expression fusion construct containing the *M. tuberculosis* antigen Ra12 (SEQ ID NO: 819) and P775P-ORF3 with an N-terminal 6x HisTag was prepared as follows. P775P-ORF3 was amplified using the sense PCR primers of SEQ ID NO: 832 and the anti-sense PCR primer of SEQ ID NO: 833. The PCR amplified fragment of P775P and

Ra12/pCRX1 were digested with the restriction enzymes EcoRI and XhoI. Vector and insert were ligated and then transformed into NovaBlue cells. Colonies were randomly screened for insert and then sequenced. A clone having the desired sequence was transformed into *E. coli* BL21 (DE3) CodonPlus-RIL competent cells. Two hours after  
5 induction, the cell density peaked at OD600 of approximately 1.8. Coomassie stained SDS-PAGE showed an over-expressed band at about 31 kD. Western blot using 6x HisTag antibody confirmed that the band was Ra12-P775P-ORF3. The determined cDNA and amino acid sequences for the fusion construct are provided in SEQ ID NO: 834 and 835, respectively.

10

H) Expression of a P703P His tag fusion protein in *E. coli*

The cDNA for the coding region of P703P was prepared by PCR using the primers of SEQ ID NO: 836 and 837. The PCR product was digested with EcoRI restriction enzyme, gel purified and cloned into a modified pET28 vector with a His tag  
15 in frame, which had been digested with Eco72I and EcoRI restriction enzymes. The correct construct was confirmed by DNA sequence analysis and then transformed into *E. coli* BL21 (DE3) pLys S expression host cells. The determined amino acid and cDNA sequences for the expressed recombinant P703P are provided in SEQ ID NO: 838 and 839, respectively.

20

I) Expression of a P705P His tag fusion protein in *E. coli*

The cDNA for the coding region of P705P was prepared by PCR using the primers of SEQ ID NO: 840 and 841. The PCR product was digested with EcoRI restriction enzyme, gel purified and cloned into a modified pET28 vector with a His tag  
25 in frame, which had been digested with Eco72I and EcoRI restriction enzymes. The correct construct was confirmed by DNA sequence analysis and then transformed into *E. coli* BL21 (DE3) pLys S and BL21 (DE3) CodonPlus expression host cells. The determined amino acid and cDNA sequences for the expressed recombinant P705P are provided in SEQ ID NO: 842 and 843, respectively.

30

J) Expression of a P711P His tag fusion protein in *E. coli*

The cDNA for the coding region of P711P was prepared by PCR using the primers of SEQ ID NO: 844 and 845. The PCR product was digested with EcoRI restriction enzyme, gel purified and cloned into a modified pET28 vector with a His tag in frame, which had been digested with Eco72I and EcoRI restriction enzymes. The correct construct was confirmed by DNA sequence analysis and then transformed into *E. coli* BL21 (DE3) pLys S and BL21 (DE3) CodonPlus expression host cells. The determined amino acid and cDNA sequences for the expressed recombinant P711P are provided in SEQ ID NO: 846 and 847, respectively.

10

K) Expression of P767P in *E. coli*

The full-length coding region of P767P (amino acids 2-374 of SEQ ID NO: 590) was amplified by PCR using the primers PDM-468 and PDM-469 (SEQ ID NO: 935 and 936, respectively). DNA amplification was performed using 10 µl 10X Pfu buffer, 1 µl 10 mM dNTPs, 2 µl each of the PCR primers at 10 µM concentration, 83 µl water, 1.5 µl Pfu DNA polymerase (Stratagene, La Jolla, CA) and 1 µl DNA at 100 ng/µl. Denaturation at 96°C was performed for 2 min, followed by 40 cycles of 96°C for 20 sec, 66°C for 15 sec and by 72°C for 2 min., and lastly by 1 cycle of 72°C for 4 min. The PCR product was digested with XhoI and cloned into a modified pET28 vector with a histidine tag in frame on the 5' end that was digested with Eco72I and XhoI. The construct was confirmed to be correct through sequence analysis and transformed into *E. coli* BL21 pLysS and BL21 CodonPlus RP cells. The cDNA coding region for the recombinant B767P protein is provided in SEQ ID NO: 938, with the corresponding amino acid sequence being provided in SEQ ID NO: 941. The full-length P767P did not express at high enough levels for detection or purification.

25

A truncated coding region of P767P (referred to as B767P-B; amino acids 47-374 of SEQ ID NO: 590) was amplified by PCR using the primers PDM-573 and PDM-469 (SEQ ID NO: 937 and 936, respectively) and the PCR conditions described above for full-length P767P. The PCR product was digested with XhoI and cloned into the modified pET28 vector that was digested with Eco72I and XhoI. The

30

construct was confirmed to be correct through sequence analysis and transformed into *E. coli* BL21 pLysS and BL21 CodonPlus RP cells. The protein was found to be expressed in the inclusion body pellet. The coding region for the expressed B767P-B protein is provided in SEQ ID NO: 939, with the corresponding amino acid sequence  
5 being provided in SEQ ID NO: 940.

### EXAMPLE 18

#### PREPARATION AND CHARACTERIZATION OF ANTIBODIES AGAINST PROSTATE-SPECIFIC POLYPEPTIDES

10

##### a) Preparation and Characterization of Polyclonal Antibodies against P703P, P504S and P509S

Polyclonal antibodies against P703P, P504S and P509S were prepared as follows.

15 Each prostate tumor antigen expressed in an *E. coli* recombinant expression system was grown overnight in LB broth with the appropriate antibiotics at 37°C in a shaking incubator. The next morning, 10 ml of the overnight culture was added to 500 ml to 2x YT plus appropriate antibiotics in a 2L-baffled Erlenmeyer flask. When the Optical Density (at 560 nm) of the culture reached 0.4-0.6, the cells were  
20 induced with IPTG (1 mM). Four hours after induction with IPTG, the cells were harvested by centrifugation. The cells were then washed with phosphate buffered saline and centrifuged again. The supernatant was discarded and the cells were either frozen for future use or immediately processed. Twenty ml of lysis buffer was added to the cell pellets and vortexed. To break open the *E. coli* cells, this mixture was then run  
25 through the French Press at a pressure of 16,000 psi. The cells were then centrifuged again and the supernatant and pellet were checked by SDS-PAGE for the partitioning of the recombinant protein. For proteins that localized to the cell pellet, the pellet was resuspended in 10 mM Tris pH 8.0, 1% CHAPS and the inclusion body pellet was washed and centrifuged again. This procedure was repeated twice more. The washed

inclusion body pellet was solubilized with either 8 M urea or 6 M guanidine HCl containing 10 mM Tris pH 8.0 plus 10 mM imidazole. The solubilized protein was added to 5 ml of nickel-chelate resin (Qiagen) and incubated for 45 min to 1 hour at room temperature with continuous agitation. After incubation, the resin and protein mixture were poured through a disposable column and the flow through was collected. The column was then washed with 10-20 column volumes of the solubilization buffer. The antigen was then eluted from the column using 8M urea, 10 mM Tris pH 8.0 and 300 mM imidazole and collected in 3 ml fractions. A SDS-PAGE gel was run to determine which fractions to pool for further purification.

10           As a final purification step, a strong anion exchange resin such as HiPrepQ (Biorad) was equilibrated with the appropriate buffer and the pooled fractions from above were loaded onto the column. Each antigen was eluted off the column with a increasing salt gradient. Fractions were collected as the column was run and another SDS-PAGE gel was run to determine which fractions from the column to pool. The  
15           pooled fractions were dialyzed against 10 mM Tris pH 8.0. The proteins were then vialled after filtration through a 0.22 micron filter and the antigens were frozen until needed for immunization.

          Four hundred micrograms of each prostate antigen was combined with 100 micrograms of muramyl dipeptide (MDP). Every four weeks rabbits were boosted  
20           with 100 micrograms mixed with an equal volume of Incomplete Freund's Adjuvant (IFA). Seven days following each boost, the animal was bled. Sera was generated by incubating the blood at 4°C for 12-4 hours followed by centrifugation.

          Ninety-six well plates were coated with antigen by incubating with 50 microliters (typically 1 microgram) of recombinant protein at 4 °C for 20 hours. 250  
25           microliters of BSA blocking buffer was added to the wells and incubated at room temperature for 2 hours. Plates were washed 6 times with PBS/0.01% Tween. Rabbit sera was diluted in PBS. Fifty microliters of diluted sera was added to each well and incubated at room temperature for 30 min. Plates were washed as described above before 50 microliters of goat anti-rabbit horse radish peroxidase (HRP) at a 1:10000  
30           dilution was added and incubated at room temperature for 30 min. Plates were again

washed as described above and 100 microliters of TMB microwell peroxidase substrate was added to each well. Following a 15 min incubation in the dark at room temperature, the colorimetric reaction was stopped with 100 microliters of 1N H<sub>2</sub>SO<sub>4</sub> and read immediately at 450 nm. All polyclonal antibodies showed immunoreactivity to the appropriate antigen.

b) Preparation and Characterization of Antibodies against P501S

A murine monoclonal antibody directed against the carboxy-terminus of the prostate-specific antigen P501S was prepared as follows.

A truncated fragment of P501S (amino acids 355-526 of SEQ ID NO: 113) was generated and cloned into the pET28b vector (Novagen) and expressed in *E. coli* as a thioredoxin fusion protein with a histidine tag. The trx-P501S fusion protein was purified by nickel chromatography, digested with thrombin to remove the trx fragment and further purified by an acid precipitation procedure followed by reverse phase HPLC.

Mice were immunized with truncated P501S protein. Serum bleeds from mice that potentially contained anti-P501S polyclonal sera were tested for P501S-specific reactivity using ELISA assays with purified P501S and trx-P501S proteins. Serum bleeds that appeared to react specifically with P501S were then screened for P501S reactivity by Western analysis. Mice that contained a P501S-specific antibody component were sacrificed and spleen cells were used to generate anti-P501S antibody producing hybridomas using standard techniques. Hybridoma supernatants were tested for P501S-specific reactivity initially by ELISA, and subsequently by FACS analysis of reactivity with P501S transduced cells. Based on these results, a monoclonal hybridoma referred to as 10E3 was chosen for further subcloning. A number of subclones were generated, tested for specific reactivity to P501S using ELISA and typed for IgG isotype. The results of this analysis are shown below in Table V. Of the 16 subclones tested, the monoclonal antibody 10E3-G4-D3 was selected for further study.



Table V

Isotype analysis of murine anti-P501S monoclonal antibodies

Hybridoma clone	Isotype	Estimated [Ig] in supernatant ( $\mu\text{g/ml}$ )
4D11	IgG1	14.6
1G1	IgG1	0.6
4F6	IgG1	72
4H5	IgG1	13.8
4H5-E12	IgG1	10.7
4H5-EH2	IgG1	9.2
4H5-H2-A10	IgG1	10
4H5-H2-A3	IgG1	12.8
4H5-H2-A10-G6	IgG1	13.6
4H5-H2-B11	IgG1	12.3
10E3	IgG2a	3.4
10E3-D4	IgG2a	3.8
10E3-D4-G3	IgG2a	9.5
10E3-D4-G6	IgG2a	10.4
10E3-E7	IgG2a	6.5
8H12	IgG2a	0.6

- 5           The specificity of 10E3-G4-D3 for P501S was examined by FACS analysis. Specifically, cells were fixed (2% formaldehyde, 10 minutes), permeabilized (0.1% saponin, 10 minutes) and stained with 10E3-G4-D3 at 0.5 – 1  $\mu\text{g/ml}$ , followed by incubation with a secondary, FITC-conjugated goat anti-mouse Ig antibody (Pharmingen, San Diego, CA). Cells were then analyzed for FITC fluorescence using
- 10 an Excalibur fluorescence activated cell sorter. For FACS analysis of transduced cells, B-LCL were retrovirally transduced with P501S. For analysis of infected cells, B-LCL were infected with a vaccinia vector that expresses P501S. To demonstrate specificity in these assays, B-LCL transduced with a different antigen (P703P) and uninfected B-LCL vectors were utilized. 10E3-G4-D3 was shown to bind with P501S-transduced B-
- 15 LCL and also with P501S-infected B-LCL, but not with either uninfected cells or P703P-transduced cells.

To determine whether the epitope recognized by 10E3-G4-D3 was found on the surface or in an intracellular compartment of cells, B-LCL were transduced with P501S or HLA-B8 as a control antigen and either fixed and permeabilized as described

above or directly stained with 10E3-G4-D3 and analyzed as above. Specific recognition of P501S by 10E3-G4-D3 was found to require permeabilization, suggesting that the epitope recognized by this antibody is intracellular.

The reactivity of 10E3-G4-D3 with the three prostate tumor cell lines Lncap, PC-3 and DU-145, which are known to express high, medium and very low levels of P501S, respectively, was examined by permeabilizing the cells and treating them as described above. Higher reactivity of 10E3-G4-D3 was seen with Lncap than with PC-3, which in turn showed higher reactivity than DU-145. These results are in agreement with the real time PCR and demonstrate that the antibody specifically recognizes P501S in these tumor cell lines and that the epitope recognized in prostate tumor cell lines is also intracellular.

Specificity of 10E3-G4-D3 for P501S was also demonstrated by Western blot analysis. Lysates from the prostate tumor cell lines Lncap, DU-145 and PC-3, from P501S-transiently transfected HEK293 cells, and from non-transfected HEK293 cells were generated. Western blot analysis of these lysates with 10E3-G4-D3 revealed a 46 kDa immunoreactive band in Lncap, PC-3 and P501S-transfected HEK cells, but not in DU-145 cells or non-transfected HEK293 cells. P501S mRNA expression is consistent with these results since semi-quantitative PCR analysis revealed that P501S mRNA is expressed in Lncap, to a lesser but detectable level in PC-3 and not at all in DU-145 cells. Bacterially expressed and purified recombinant P501S (referred to as P501SStr2) was recognized by 10E3-G4-D3 (24 kDa), as was full-length P501S that was transiently expressed in HEK293 cells using either the expression vector VR1012 or pCEP4. Although the predicted molecular weight of P501S is 60.5 kDa, both transfected and "native" P501S run at a slightly lower mobility due to its hydrophobic nature.

Immunohistochemical analysis was performed on prostate tumor and a panel of normal tissue sections (prostate, adrenal, breast, cervix, colon, duodenum, gall bladder, ileum, kidney, ovary, pancreas, parotid gland, skeletal muscle, spleen and testis). Tissue samples were fixed in formalin solution for 24 hours and embedded in paraffin before being sliced into 10 micron sections. Tissue sections were permeabilized and incubated with 10E3-G4-D3 antibody for 1 hr. HRP-labeled anti-

mouse followed by incubation with DAB chromogen was used to visualize P501S immunoreactivity. P501S was found to be highly expressed in both normal prostate and prostate tumor tissue but was not detected in any of the other tissues tested.

To identify the epitope recognized by 10E3-G4-D3, an epitope mapping approach was pursued. A series of 13 overlapping 20-21 mers (5 amino acid overlap; SEQ ID NO: 489-501) was synthesized that spanned the fragment of P501S used to generate 10E3-G4-D3. Flat bottom 96 well microtiter plates were coated with either the peptides or the P501S fragment used to immunize mice, at 1 microgram/ml for 2 hours at 37 °C. Wells were then aspirated and blocked with phosphate buffered saline containing 1% (w/v) BSA for 2 hours at room temperature, and subsequently washed in PBS containing 0.1% Tween 20 (PBST). Purified antibody 10E3-G4-D3 was added at 2 fold dilutions (1000 ng – 16 ng) in PBST and incubated for 30 minutes at room temperature. This was followed by washing 6 times with PBST and subsequently incubating with HRP-conjugated donkey anti-mouse IgG (H+L) Affinipure F(ab') fragment (Jackson ImmunoResearch, West Grove, PA) at 1:20000 for 30 minutes. Plates were then washed and incubated for 15 minutes in tetramethyl benzidine. Reactions were stopped by the addition of 1N sulfuric acid and plates were read at 450 nm using an ELISA plate reader. As shown in Fig. 8, reactivity was seen with the peptide of SEQ ID NO: 496 (corresponding to amino acids 439-459 of P501S) and with the P501S fragment but not with the remaining peptides, demonstrating that the epitope recognized by 10E3-G4-D3 is localized to amino acids 439-459 of SEQ ID NO: 113.

In order to further evaluate the tissue specificity of P501S, multi-array immunohistochemical analysis was performed on approximately 4700 different human tissues encompassing all the major normal organs as well as neoplasias derived from these tissues. Sixty-five of these human tissue samples were of prostate origin. Tissue sections 0.6 mm in diameter were formalin-fixed and paraffin embedded. Samples were pretreated with HIER using 10 mM citrate buffer pH 6.0 and boiling for 10 min. Sections were stained with 10E3-G4-D3 and P501S immunoreactivity was visualized with HRP. All the 65 prostate tissues samples (5 normal, 55 untreated prostate tumors,

5 hormone refractory prostate tumors) were positive, showing distinct perinuclear staining. All other tissues examined were negative for P501S expression.

c) Preparation and Characterization of Antibodies against P503S

5 A fragment of P503S (amino acids 113-241 of SEQ ID NO: 114) was expressed and purified from bacteria essentially as described above for P501S and used to immunize both rabbits and mice. Mouse monoclonal antibodies were isolated using standard hybridoma technology as described above. Rabbit monoclonal antibodies were isolated using Selected Lymphocyte Antibody Method (SLAM) technology at  
 10 Immgenics Pharmaceuticals (Vancouver, BC, Canada). Table VI, below, lists the monoclonal antibodies that were developed against P503S.

Table VI

Antibody	Species
20D4	Rabbit
JA1	Rabbit
1A4	Mouse
1C3	Mouse
1C9	Mouse
1D12	Mouse
2A11	Mouse
2H9	Mouse
4H7	Mouse
8A8	Mouse
8D10	Mouse
9C12	Mouse
6D12	Mouse

15

The DNA sequences encoding the complementarity determining regions (CDRs) for the rabbit monoclonal antibodies 20D4 and JA1 were determined and are provided in SEQ ID NO: 502 and 503, respectively.

In order to better define the epitope binding region of each of the antibodies, a series of overlapping peptides were generated that span amino acids 109-213 of SEQ ID NO: 114. These peptides were used to epitope map the anti-P503S monoclonal antibodies by ELISA as follows. The recombinant fragment of P503S that was employed as the immunogen was used as a positive control. Ninety-six well microtiter plates were coated with either peptide or recombinant antigen at 20 ng/well overnight at 4 °C. Plates were aspirated and blocked with phosphate buffered saline containing 1% (w/v) BSA for 2 hours at room temperature then washed in PBS containing 0.1% Tween 20 (PBST). Purified rabbit monoclonal antibodies diluted in PBST were added to the wells and incubated for 30 min at room temperature. This was followed by washing 6 times with PBST and incubation with Protein-A HRP conjugate at a 1:2000 dilution for a further 30 min. Plates were washed six times in PBST and incubated with tetramethylbenzidine (TMB) substrate for a further 15 min. The reaction was stopped by the addition of 1N sulfuric acid and plates were read at 450 nm using an ELISA plate reader. ELISA with the mouse monoclonal antibodies was performed with supernatants from tissue culture run neat in the assay.

All of the antibodies bound to the recombinant P503S fragment, with the exception of the negative control SP2 supernatant. 20D4, JA1 and 1D12 bound strictly to peptide #2101 (SEQ ID NO: 504), which corresponds to amino acids 151-169 of SEQ ID NO: 114. 1C3 bound to peptide #2102 (SEQ ID NO: 505), which corresponds to amino acids 165-184 of SEQ ID NO: 114. 9C12 bound to peptide #2099 (SEQ ID NO: 522), which corresponds to amino acids 120-139 of SEQ ID NO: 114. The other antibodies bind to regions that were not examined in these studies.

Subsequent to epitope mapping, the antibodies were tested by FACS analysis on a cell line that stably expressed P503S to confirm that the antibodies bind to cell surface epitopes. Cells stably transfected with a control plasmid were employed as a negative control. Cells were stained live with no fixative. 0.5 ug of anti-P503S monoclonal antibody was added and cells were incubated on ice for 30 min before being washed twice and incubated with a FITC-labelled goat anti-rabbit or mouse secondary antibody for 20 min. After being washed twice, cells were analyzed with an Excalibur

fluorescent activated cell sorter. The monoclonal antibodies 1C3, 1D12, 9C12, 20D4 and JA1, but not 8D3, were found to bind to a cell surface epitope of P503S.

In order to determine which tissues express P503S, immunohistochemical analysis was performed, essentially as described above, on a panel of normal tissues (prostate, adrenal, breast, cervix, colon, duodenum, gall bladder, ileum, kidney, ovary, pancreas, parotid gland, skeletal muscle, spleen and testis). HRP-labeled anti-mouse or anti-rabbit antibody followed by incubation with TMB was used to visualize P503S immunoreactivity. P503S was found to be highly expressed in prostate tissue, with lower levels of expression being observed in cervix, colon, ileum and kidney, and no expression being observed in adrenal, breast, duodenum, gall bladder, ovary, pancreas, parotid gland, skeletal muscle, spleen and testis.

Western blot analysis was used to characterize anti-P503S monoclonal antibody specificity. SDS-PAGE was performed on recombinant (rec) P503S expressed in and purified from bacteria and on lysates from HEK293 cells transfected with full length P503S. Protein was transferred to nitrocellulose and then Western blotted with each of the anti-P503S monoclonal antibodies (20D4, JA1, 1D12, 6D12 and 9C12) at an antibody concentration of 1 ug/ml. Protein was detected using horse radish peroxidase (HRP) conjugated to either a goat anti-mouse monoclonal antibody or to protein A-sepharose. The monoclonal antibody 20D4 detected the appropriate molecular weight 14 kDa recombinant P503S (amino acids 113-241) and the 23.5 kDa species in the HEK293 cell lysates transfected with full length P503S. Other anti-P503S monoclonal antibodies displayed similar specificity by Western blot.

#### d) Preparation and Characterization of Antibodies against P703P

Rabbits were immunized with either a truncated (P703Ptr1; SEQ ID NO: 172) or full-length mature form (P703Pfl; SEQ ID NO: 523) of recombinant P703P protein was expressed in and purified from bacteria as described above. Affinity purified polyclonal antibody was generated using immunogen P703Pfl or P703Ptr1 attached to a solid support. Rabbit monoclonal antibodies were isolated using SLAM

technology at Immgenics Pharmaceuticals. Table VII below lists both the polyclonal and monoclonal antibodies that were generated against P703P.

Table VII

5

Antibody	Immunogen	Species/type
Aff. Purif. P703P (truncated); #2594	P703Ptrl	Rabbit polyclonal
Aff. Purif. P703P (full length); #9245	P703Pfl	Rabbit polyclonal
2D4	P703Ptrl	Rabbit monoclonal
8H2	P703Ptrl	Rabbit monoclonal
7H8	P703Ptrl	Rabbit monoclonal

The DNA sequences encoding the complementarity determining regions (CDRs) for the rabbit monoclonal antibodies 8H2, 7H8 and 2D4 were determined and are provided in SEQ ID NO: 506-508, respectively.

10

Epitope mapping studies were performed as described above. Monoclonal antibodies 2D4 and 7H8 were found to specifically bind to the peptides of SEQ ID NO: 509 (corresponding to amino acids 145-159 of SEQ ID NO: 172) and SEQ ID NO: 510 (corresponding to amino acids 11-25 of SEQ ID NO: 172), respectively. The polyclonal antibody 2594 was found to bind to the peptides of SEQ ID NO: 511-  
 15 514, with the polyclonal antibody 9427 binding to the peptides of SEQ ID NO: 515-517.

20

The specificity of the anti-P703P antibodies was determined by Western blot analysis as follows. SDS-PAGE was performed on (1) bacterially expressed recombinant antigen; (2) lysates of HEK293 cells and Ltk<sup>-/-</sup> cells either untransfected or transfected with a plasmid expressing full length P703P; and (3) supernatant isolated  
 25 from these cell cultures. Protein was transferred to nitrocellulose and then Western blotted using the anti-P703P polyclonal antibody #2594 at an antibody concentration of 1 ug/ml. Protein was detected using horse radish peroxidase (HRP) conjugated to an anti-rabbit antibody. A 35 kDa immunoreactive band could be observed with recombinant P703P. Recombinant P703P runs at a slightly higher molecular weight since it is epitope tagged. In lysates and supernatants from cells transfected with full length P703P, a 30 kDa band corresponding to P703P was observed. To assure

specificity, lysates from HEK293 cells stably transfected with a control plasmid were also tested and were negative for P703P expression. Other anti-P703P antibodies showed similar results.

- Immunohistochemical studies were performed as described above, using
- 5 anti-P703P monoclonal antibody. P703P was found to be expressed at high levels in normal prostate and prostate tumor tissue but was not detectable in all other tissues tested (breast tumor, lung tumor and normal kidney).

e) Preparation and Characterization of Antibodies against P504S

- Full-length P504S (SEQ ID NO: 108) was expressed and purified from
- 10 bacteria essentially as described above for P501S and employed to raise rabbit monoclonal antibodies using Selected Lymphocyte Antibody Method (SLAM) technology at Immgenics Pharmaceuticals (Vancouver, BC, Canada). The anti-P504S monoclonal antibody 13H4 was shown by Western blot to bind to both expressed recombinant P504S and to native P504S in tumor cells.

- 15 Immunohistochemical studies using 13H4 to assess P504S expression in various prostate tissues were performed as described above. A total of 104 cases, including 65 cases of radical prostatectomies with prostate cancer (PC), 26 cases of prostate biopsies and 13 cases of benign prostate hyperplasia (BPH), were stained with the anti-P504S monoclonal antibody 13H4. P504S showed strongly cytoplasmic
- 20 granular staining in 64/65 (98.5%) of PCs in prostatectomies and 26/26 (100%) of PCs in prostatic biopsies. P504S was stained strongly and diffusely in carcinomas (4+ in 91.2% of cases of PC; 3+ in 5.5%; 2+ in 2.2% and 1+ in 1.1%) and high grade prostatic intraepithelial neoplasia (4+ in all cases). The expression of P504S did not vary with Gleason score. Only 17/91 (18.7%) of cases of NP/BPH around PC and 2/13 (15.4%) of
- 25 BPH cases were focally (1+, no 2+ to 4+ in all cases) and weakly positive for P504S in large glands. Expression of P504S was not found in small atrophic glands, postatrophic hyperplasia, basal cell hyperplasia and transitional cell metaplasia in either biopsies or prostatectomies. P504S was thus found to be over-expressed in all Gleason scores of prostate cancer (98.5 to 100% of sensitivity) and exhibited only focal positivities in



large normal glands in 19/104 of cases (82.3% of specificity). These findings indicate that P504S may be usefully employed for the diagnosis of prostate cancer.

### EXAMPLE 19

#### 5 CHARACTERIZATION OF CELL SURFACE EXPRESSION AND CHROMOSOME LOCALIZATION OF THE PROSTATE-SPECIFIC ANTIGEN P501S

This example describes studies demonstrating that the prostate-specific antigen P501S is expressed on the surface of cells, together with studies to determine  
10 the probable chromosomal location of P501S.

The protein P501S (SEQ ID NO: 113) is predicted to have 11 transmembrane domains. Based on the discovery that the epitope recognized by the anti-P501S monoclonal antibody 10E3-G4-D3 (described above in Example 17) is intracellular, it was predicted that following transmembrane determinants would allow  
15 the prediction of extracellular domains of P501S. Fig. 9 is a schematic representation of the P501S protein showing the predicted location of the transmembrane domains and the intracellular epitope described in Example 17. Underlined sequence represents the predicted transmembrane domains, bold sequence represents the predicted extracellular domains, and italicized sequence represents the predicted intracellular domains.  
20 Sequence that is both bold and underlined represents sequence employed to generate polyclonal rabbit serum. The location of the transmembrane domains was predicted using HHMTOP as described by Tusnady and Simon (Principles Governing Amino Acid Composition of Integral Membrane Proteins: Applications to Topology Prediction, *J. Mol. Biol.* 283:489-506, 1998).

25 Based on Fig. 9, the P501S domain flanked by the transmembrane domains corresponding to amino acids 274-295 and 323-342 is predicted to be extracellular. The peptide of SEQ ID NO: 518 corresponds to amino acids 306-320 of P501S and lies in the predicted extracellular domain. The peptide of SEQ ID NO: 519, which is identical to the peptide of SEQ ID NO: 518 with the exception of the  
30 substitution of the histidine with an asparagine, was synthesized as described above. A

Cys-Gly was added to the C-terminus of the peptide to facilitate conjugation to the carrier protein. Cleavage of the peptide from the solid support was carried out using the following cleavage mixture: trifluoroacetic acid:ethanediol:thioanisol:water:phenol (40:1:2:2:3). After cleaving for two hours, the peptide was precipitated in cold ether.

5 The peptide pellet was then dissolved in 10% v/v acetic acid and lyophilized prior to purification by C18 reverse phase hplc. A gradient of 5-60% acetonitrile (containing 0.05% TFA) in water (containing 0.05% TFA) was used to elute the peptide. The purity of the peptide was verified by hplc and mass spectrometry, and was determined to be >95%. The purified peptide was used to generate rabbit polyclonal antisera as described

10 above.

Surface expression of P501S was examined by FACS analysis. Cells were stained with the polyclonal anti-P501S peptide serum at 10 µg/ml, washed, incubated with a secondary FITC-conjugated goat anti-rabbit Ig antibody (ICN), washed and analyzed for FITC fluorescence using an Excalibur fluorescence activated cell

15 sorter. For FACS analysis of transduced cells, B-LCL were retrovirally transduced with P501S. To demonstrate specificity in these assays, B-LCL transduced with an irrelevant antigen (P703P) or nontransduced were stained in parallel. For FACS analysis of prostate tumor cell lines, Lncap, PC-3 and DU-145 were utilized. Prostate tumor cell lines were dissociated from tissue culture plates using cell dissociation medium and

20 stained as above. All samples were treated with propidium iodide (PI) prior to FACS analysis, and data was obtained from PI-excluding (*i.e.*, intact and non-permeabilized) cells. The rabbit polyclonal serum generated against the peptide of SEQ ID NO: 519 was shown to specifically recognize the surface of cells transduced to express P501S, demonstrating that the epitope recognized by the polyclonal serum is extracellular.

25 To determine biochemically if P501S is expressed on the cell surface, peripheral membranes from Lncap cells were isolated and subjected to Western blot analysis. Specifically, Lncap cells were lysed using a dounce homogenizer in 5 ml of homogenization buffer (250 mM sucrose, 10 mM HEPES, 1mM EDTA, pH 8.0, 1 complete protease inhibitor tablet (Boehringer Mannheim)). Lysate samples were spun

30 at 1000 g for 5 min at 4 °C. The supernatant was then spun at 8000g for 10 min at 4 °C.

Supernatant from the 8000g spin was recovered and subjected to a 100,000g spin for 30 min at 4 °C to recover peripheral membrane. Samples were then separated by SDS-PAGE and Western blotted with the mouse monoclonal antibody 10E3-G4-D3 (described above in Example 17) using conditions described above. Recombinant  
5 purified P501S, as well as HEK293 cells transfected with and over-expressing P501S were included as positive controls for P501S detection. LCL cell lysate was included as a negative control. P501S could be detected in Lncap total cell lysate, the 8000g (internal membrane) fraction and also in the 100,000g (plasma membrane) fraction. These results indicate that P501S is expressed at, and localizes to, the peripheral  
10 membrane.

To demonstrate that the rabbit polyclonal antiserum generated to the peptide of SEQ ID NO: 519 specifically recognizes this peptide as well as the corresponding native peptide of SEQ ID NO: 518, ELISA analyses were performed. For these analyses, flat-bottomed 96 well microtiter plates were coated with either the  
15 peptide of SEQ ID NO: 519, the longer peptide of SEQ ID NO: 520 that spans the entire predicted extracellular domain, the peptide of SEQ ID NO: 521 which represents the epitope recognized by the P501S-specific antibody 10E3-G4-D3, or a P501S fragment (corresponding to amino acids 355-526 of SEQ ID NO: 113) that does not include the immunizing peptide sequence, at 1 µg/ml for 2 hours at 37 °C. Wells were aspirated,  
20 blocked with phosphate buffered saline containing 1% (w/v) BSA for 2 hours at room temperature and subsequently washed in PBS containing 0.1% Tween 20 (PBST). Purified anti-P501S polyclonal rabbit serum was added at 2 fold dilutions (1000 ng - 125 ng) in PBST and incubated for 30 min at room temperature. This was followed by washing 6 times with PBST and incubating with HRP-conjugated goat anti-rabbit IgG  
25 (H+L) Affinipure F(ab') fragment at 1:20000 for 30 min. Plates were then washed and incubated for 15 min in tetramethyl benzidine. Reactions were stopped by the addition of 1N sulfuric acid and plates were read at 450 nm using an ELISA plate reader. As shown in Fig. 11, the anti-P501S polyclonal rabbit serum specifically recognized the peptide of SEQ ID NO: 519 used in the immunization as well as the longer peptide of

SEQ ID NO: 520, but did not recognize the irrelevant P501S-derived peptides and fragments.

In further studies, rabbits were immunized with peptides derived from the P501S sequence and predicted to be either extracellular or intracellular, as shown in Fig. 9. Polyclonal rabbit sera were isolated and polyclonal antibodies in the serum were purified, as described above. To determine specific reactivity with P501S, FACS analysis was employed, utilizing either B-LCL transduced with P501S or the irrelevant antigen P703P, of B-LCL infected with vaccinia virus-expressing P501S. For surface expression, dead and non-intact cells were excluded from the analysis as described above. For intracellular staining, cells were fixed and permeabilized as described above. Rabbit polyclonal serum generated against the peptide of SEQ ID NO: 548, which corresponds to amino acids 181-198 of P501S, was found to recognize a surface epitope of P501S. Rabbit polyclonal serum generated against the peptide SEQ ID NO: 551, which corresponds to amino acids 543-553 of P501S, was found to recognize an epitope that was either potentially extracellular or intracellular since in different experiments intact or permeabilized cells were recognized by the polyclonal sera. Based on similar deductive reasoning, the sequences of SEQ ID NO: 541-547, 549 and 550, which correspond to amino acids 109-122, 539-553, 509-520, 37-54, 342-359, 295-323, 217-274, 143-160 and 75-88, respectively, of P501S, can be considered to be potential surface epitopes of P501S recognized by antibodies.

In further studies, mouse monoclonal antibodies were raised against amino acids 296 to 322 to P501S, which are predicted to be in an extracellular domain. A/J mice were immunized with P501S/adenovirus, followed by subsequent boosts with an *E. coli* recombinant protein, referred to as P501N, that contains amino acids 296 to 322 of P501S, and with peptide 296-322 (SEQ ID NO: 898) coupled with KLH. The mice were subsequently used for splenic B cell fusions to generate anti-peptide hybridomas. The resulting 3 clones, referred to as 4F4 (IgG1,kappa), 4G5 (IgG2a,kappa) and 9B9 (IgG1,kappa), were grown for antibody production. The 4G5 mAb was purified by passing the supernatant over a Protein A-sepharose column,

followed by antibody elution using 0.2M glycine, pH 2.3. Purified antibody was neutralized by the addition of 1M Tris, pH 8, and buffer exchanged into PBS.

For ELISA analysis, 96 well plates were coated with P501S peptide 296-322 (referred to as P501-long), an irrelevant P775 peptide, P501S-N, P501TR2, P501S-long-KLH, P501S peptide 306-319 (referred to as P501-short)-KLH, or the irrelevant peptide 2073-KLH, all at a concentration of 2 ug/ml and allowed to incubate for 60 minutes at 37 °C. After coating, plates were washed 5X with PBS + 0.1% Tween and then blocked with PBS, 0.5% BSA, 0.4% Tween20 for 2 hours at room temperature. Following the addition of supernatants or purified mAb, the plates were incubated for 60 minutes at room temperature. Plates were washed as above and donkey anti-mouse IgHRP-linked secondary antibody was added and incubated for 30 minutes at room temperature, followed by a final washing as above. TMB peroxidase substrate was added and incubated 15 minutes at room temperature in the dark. The reaction was stopped by the addition of 1N H<sub>2</sub>SO<sub>4</sub> and the OD was read at 450 nM. All three hybrid clones secreted mAb that recognized peptide 296-322 and the recombinant protein P501N.

For FACS analysis, HEK293 cells were transiently transfected with a P501S/VR1012 expression constructs using Fugene 6 reagent. After 2 days of culture, cells were harvested and washed, then incubated with purified 4G5 mAb for 30 minutes on ice. After several washes in PBS, 0.5% BSA, 0.01% azide, goat anti-mouse Ig-FITC was added to the cells and incubated for 30 minutes on ice. Cells were washed and resuspended in wash buffer including 1% propidium iodide and subjected to FACS analysis. The FACS analysis confirmed that amino acids 296-322 of P501S are in an extracellular domain and are cell surface expressed.

The chromosomal location of P501S was determined using the GeneBridge 4 Radiation Hybrid panel (Research Genetics). The PCR primers of SEQ ID NO: 528 and 529 were employed in PCR with DNA pools from the hybrid panel according to the manufacturer's directions. After 38 cycles of amplification, the reaction products were separated on a 1.2% agarose gel, and the results were analyzed through the Whitehead Institute/MIT Center for Genome Research web server

(<http://www-genome.wi.mit.edu/cgi-bin/contig/rhmapper.pl>) to determine the probable chromosomal location. Using this approach, P501S was mapped to the long arm of chromosome 1 at WI-9641 between q32 and q42. This region of chromosome 1 has been linked to prostate cancer susceptibility in hereditary prostate cancer (Smith *et al.* 5 *Science* 274:1371-1374, 1996 and Berthon *et al. Am. J. Hum. Genet.* 62:1416-1424, 1998). These results suggest that P501S may play a role in prostate cancer malignancy.

#### EXAMPLE 20

##### REGULATION OF EXPRESSION OF THE PROSTATE-SPECIFIC ANTIGEN P501S

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Steroid (androgen) hormone modulation is a common treatment modality in prostate cancer. The expression of a number of prostate tissue-specific antigens have previously been demonstrated to respond to androgen. The responsiveness of the prostate-specific antigen P501S to androgen treatment was examined in a tissue culture 15 system as follows.

Cells from the prostate tumor cell line LNCaP were plated at  $1.5 \times 10^6$  cells/T75 flask (for RNA isolation) or  $3 \times 10^5$  cells/well of a 6-well plate (for FACS analysis) and grown overnight in RPMI 1640 media containing 10% charcoal-stripped fetal calf serum (BRL Life Technologies, Gaithersburg, MD). Cell culture was 20 continued for an additional 72 hours in RPMI 1640 media containing 10% charcoal-stripped fetal calf serum, with 1 nM of the synthetic androgen Methyltrienolone (R1881; New England Nuclear) added at various time points. Cells were then harvested for RNA isolation and FACS analysis at 0, 1, 2, 4, 8, 16, 24, 28 and 72-hours post androgen addition. FACS analysis was performed using the anti-P501S antibody 10E3- 25 G4-D3 and permeabilized cells.

For Northern analysis, 5-10 micrograms of total RNA was run on a formaldehyde denaturing gel, transferred to Hybond-N nylon membrane (Amersham Pharmacia Biotech, Piscataway, NJ), cross-linked and stained with methylene blue. The filter was then prehybridized with Church's Buffer (250 mM  $\text{Na}_2\text{HPO}_4$ , 70 mM  $\text{H}_3\text{PO}_4$ , 30 1 mM EDTA, 1% SDS, 1% BSA in pH 7.2) at 65 °C for 1 hour. P501S DNA was

labeled with  $^{32}\text{P}$  using High Prime random-primed DNA labeling kit (Boehringer Mannheim). Unincorporated label was removed using MicroSpin S300-HR columns (Amersham Pharmacia Biotech). The RNA filter was then hybridized with fresh Church's Buffer containing labeled cDNA overnight, washed with 1X SCP (0.1 M NaCl, 0.03 M  $\text{Na}_2\text{HPO}_4 \cdot 7\text{H}_2\text{O}$ , 0.001 M  $\text{Na}_2\text{EDTA}$ ), 1% sarkosyl (n-lauroylsarcosine) and exposed to X-ray film.

Using both FACS and Northern analysis, P501S message and protein levels were found to increase in response to androgen treatment.

10

## EXAMPLE 21

## PREPARATION OF FUSION PROTEINS OF PROSTATE-SPECIFIC ANTIGENS

The example describes the preparation of a fusion protein of the prostate-specific antigen P703P and a truncated form of the known prostate antigen PSA. The truncated form of PSA has a 21 amino acid deletion around the active serine site. The expression construct for the fusion protein also has a restriction site at 3' end, immediately prior to the termination codon, to aid in adding cDNA for additional antigens.

The full-length cDNA for PSA was obtained by RT-PCR from a pool of RNA from human prostate tumor tissues using the primers of SEQ ID NO: 607 and 608, and cloned in the vector pCR-Blunt II-TOPO. The resulting cDNA was employed as a template to make two different fragments of PSA by PCR with two sets of primers (SEQ ID NO: 609 and 610; and SEQ ID NO: 611 and 612). The PCR products having the expected size were used as templates to make truncated forms of PSA by PCR with the primers of SEQ ID NO: 611 and 613, which generated PSA (delta 208-218 in amino acids). The cDNA for the mature form of P703P with a 6X histidine tag at the 5' end, was prepared by PCR with P703P and the primers of SEQ ID NO: 614 and 615. The cDNA for the fusion of P703P with the truncated form of PSA (referred to as FOPP) was then obtained by PCR using the modified P703P cDNA and the truncated form of PSA cDNA as templates and the primers of SEQ ID NO: 614 and 615. The FOPP

cDNA was cloned into the NdeI site and XhoI site of the expression vector pCRX1, and confirmed by DNA sequencing. The determined cDNA sequence for the fusion construct FOPP is provided in SEQ ID NO: 616, with the amino acid sequence being provided in SEQ ID NO: 617.

5           The fusion FOPP was expressed as a single recombinant protein in *E. coli* as follows. The expression plasmid pCRX1FOPP was transformed into the *E. coli* strain BL21-CodonPlus RIL. The transformant was shown to express FOPP protein upon induction with 1 mM IPTG. The culture of the corresponding expression clone was inoculated into 25 ml LB broth containing 50 ug/ml kanamycin and 34 ug/ml  
10 chloramphenicol, grown at 37 °C to OD600 of about 1, and stored at 4 °C overnight. The culture was diluted into 1 liter of TB LB containing 50 ug/ml kanamycin and 34 ug/ml chloramphenicol, and grown at 37 °C to OD600 of 0.4. IPTG was added to a final concentration of 1 mM, and the culture was incubated at 30 °C for 3 hours. The cells were pelleted by centrifugation at 5,000 RPM for 8 min. To purify the protein, the  
15 cell pellet was suspended in 25 ml of 10 mM Tris-Cl pH 8.0, 2mM PMSF, complete protease inhibitor and 15 ug lysozyme. The cells were lysed at 4 °C for 30 minutes, sonicated several times and the lysate centrifuged for 30 minutes at 10,000 x g. The precipitate, which contained the inclusion body, was washed twice with 10 mM Tris-Cl pH 8.0 and 1% CHAPS. The inclusion body was dissolved in 40 ml of 10 mM Tris-Cl  
20 pH 8.0, 100 mM sodium phosphate and 8 M urea. The solution was bound to 8 ml Ni-NTA (Qiagen) for one hour at room temperature. The mixture was poured into a 25 ml column and washed with 50 ml of 10 mM Tris-Cl pH 6.3, 100 mM sodium phosphate, 0.5% DOC and 8M urea. The bound protein was eluted with 350 mM imidazole, 10 mM Tris-Cl pH 8.0, 100 mM sodium phosphate and 8 M urea. The fractions containing  
25 FOPP proteins were combined and dialyzed extensively against 10 mM Tris-Cl pH 4.6, aliquoted and stored at - 70 °C.



## EXAMPLE 22

REAL-TIME PCR CHARACTERIZATION OF THE PROSTATE-SPECIFIC ANTIGEN P501S IN  
PERIPHERAL BLOOD OF PROSTATE CANCER PATIENTS

5           Circulating epithelial cells were isolated from fresh blood of normal individuals and metastatic prostate cancer patients, mRNA isolated and cDNA prepared using real-time PCR procedures. Real-time PCR was performed with the Taqman<sup>TM</sup> procedure using both gene specific primers and probes to determine the levels of gene expression.

10           Epithelial cells were enriched from blood samples using an immunomagnetic bead separation method (Dynal A.S., Oslo, Norway). Isolated cells were lysed and the magnetic beads removed. The lysate was then processed for poly A+ mRNA isolation using magnetic beads coated with Oligo(dT)25. After washing the beads in buffer, bead/poly A+ RNA samples were suspended in 10 mM Tris HCl pH 8.0

15           and subjected to reversed transcription. The resulting cDNA was subjected to real-time PCR using gene specific primers. Beta-actin content was also determined and used for normalization. Samples with P501S copies greater than the mean of the normal samples + 3 standard deviations were considered positive. Real time PCR on blood samples was performed using the Taqman<sup>TM</sup> procedure but extending to 50 cycles using

20           forward and reverse primers and probes specific for P501S. Of the eight samples tested, 6 were positive for P501S and  $\beta$ -actin signal. The remaining 2 samples had no detectable  $\beta$ -actin or P501S. No P501S signal was observed in the four normal blood samples tested.

25

## EXAMPLE 23

EXPRESSION OF THE PROSTATE-SPECIFIC ANTIGENS P703P AND P501S IN  
SCID MOUSE-PASSAGED PROSTATE TUMORS

30           When considering the effectiveness of antigens in the treatment of prostate cancer, the continued presence of the antigens in tumors during androgen

ablation therapy is important. The presence of the prostate-specific antigens P703P and P501S in prostate tumor samples grown in SCID mice in the presence of testosterone was evaluated as follows.

Two prostate tumors that had metastasized to the bone were removed  
5 from patients, implanted into SCID mice and grown in the presence of testosterone. Tumors were evaluated for mRNA expression of P703P, P501S and PSA using quantitative real time PCR with the SYBR green assay method. Expression of P703P and P501S in a prostate tumor was used as a positive control and the absence in normal intestine and normal heart as negative controls. In both cases, the specific mRNA was  
10 present in late passage tumors. Since the bone metastases were grown in the presence of testosterone, this implies that the presence of these genes would not be lost during androgen ablation therapy.

#### EXAMPLE 24

##### 15 ANTI-P503S MONOCLONAL ANTIBODY INHIBITS TUMOR GROWTH *IN VIVO*

The ability of the anti-P503S monoclonal antibody 20D4 to suppress tumor formation in mice was examined as follows.

Ten SCID mice were injected subcutaneously with HEK293 cells that expressed P503S. Five mice received 150 micrograms of 20D4 intravenously at day 0  
20 (time of tumor cell injection), day 5 and day 9. Tumor size was measured for 50 days. Of the five animals that received no 20D4, three formed detectable tumors after about 2 weeks which continued to enlarge throughout the study. In contrast, none of the five mice that received 20D4 formed tumors. These results demonstrate that the anti-P503S Mab 20D4 displays potent anti-tumor activity *in vivo*.

25

#### EXAMPLE 25

##### CHARACTERIZATION OF A T CELL RECEPTOR CLONE FROM A P501S-SPECIFIC T CELL CLONE

30 T cells have a limited lifespan. However, cloning of T cell receptor (TCR) chains and subsequent transfer essentially enables infinite propagation of the T

cell specificity. Cloning of tumor-antigen TCR chains allows the transfer of the specificity into T cells isolated from patients that share the TCR MHC-restricting allele. Such T cells could then be expanded and used in adoptive transfer settings to introduce the tumor antigen specificity into patients carrying tumors that express the antigen. T  
5 cell receptor alpha and beta chains from a CD8 T cell clone specific for the prostate-specific antigen P501S were isolated and sequenced as follows.

Total mRNA from  $2 \times 10^6$  cells from CTL clone 4E5 (described above in Example 12) was isolated using Trizol reagent and cDNA was synthesized. To determine Va and Vb sequences in this clone, a panel of Va and Vb subtype-specific  
10 primers was synthesized and used in RT-PCR reactions with cDNA generated from each of the clones. The RT-PCR reactions demonstrated that each of the clones expressed a common Vb sequence that corresponded to the Vb7 subfamily. Furthermore, using cDNA generated from the clone, the Va sequence expressed was determined to be Va6. To clone the full TCR alpha and beta chains from clone 4E5,  
15 primers were designed that spanned the initiator and terminator-coding TCR nucleotides. The primers were as follows: TCR Valpha-6 5'(sense): GGATCC---GCCGCCACC---ATGTCACCTTTCTAGCCTGCT (SEQ ID NO: 899) BamHI site Kozak TCR alpha sequence TCR alpha 3' (antisense): GTCGAC---TCAGCTGGACCACAGCCGCAG (SEQ ID NO: 900) Sall site TCR alpha constant  
20 sequence TCR Vbeta-7. 5'(sense): GGATCC---GCCGCCACC---ATGGGCTGCAGGCTGCTCT (SEQ ID NO: 901) BamHI site Kozak TCR alpha sequence TCR beta 3' (antisense): GTCGAC---TCAGAAATCCTTTCTCTTGAC (SEQ ID NO: 902) Sall site TCR beta constant sequence. Standard 35 cycle RT-PCR reactions were established using cDNA synthesized from the CTL clone and the above  
25 primers, employing the proofreading thermostable polymerase PWO (Roche, Nutley, NJ).

The resultant specific bands (approx. 850 bp for alpha and approx. 950 for beta) were ligated into the PCR blunt vector (Invitrogen) and transformed into *E. coli*. *E. coli* transformed with plasmids containing full-length alpha and beta chains  
30 were identified, and large scale preparations of the corresponding plasmids were generated. Plasmids containing full-length TCR alpha and beta chains were submitted

for sequencing. The sequencing reactions demonstrated the cloning of full-length TCR alpha and beta chains with the determined cDNA sequences for the Vb and Va chains being shown in SEQ ID NO: 903 and 904, respectively. The corresponding amino acid sequences are shown in SEQ ID NO: 905 and 906, respectively. The Va sequence was  
 5 shown by nucleotide sequence alignment to be 99% identical (347/348) to Va6.2, and the Vb to be 99% identical to Vb7 (336/338).

#### EXAMPLE 26

##### CAPTURE OF PROSTATE SPECIFIC CELLS USING

##### 10 THE PROSTATE ANTIGEN P503S

As described above, P503S is found on the surface of prostate cells. Secondary coated microsphere beads specific for mouse IgG were coupled with the purified P503S-specific monoclonal antibody 1D12. The bound P503S antibody was then used to capture HEK cells expressing recombinant P503S. This provides a model  
 15 system for prostate-specific cell capture which may be usefully employed in the detection of prostate cells in blood, and therefore in the detection of prostate cancer.

P503S-transfected HEK cells were harvested and redissolved in wash buffer (PBS, 0.1% BSA, 0.6% sodium citrate) at an appropriate volume to give at least  
 5<sup>4</sup> cells per sample. Round bottom Eppendorf tubes were used for all procedures  
 20 involving beads. The stock concentrations were as shown below in Table VIII.

Table VIII

Stock concentrations	Sample concentration	Amount needed
Epithelial enrich beads 4 <sup>8</sup> beads/ml (DynaL Biotech Inc. Lake Success, NY)	1 <sup>7</sup> beads/ml	125 ul stock per 5 ml volume
1D12 ascites antibody 2 mg/ml	0.1 ug/ml (0.1X) to 5 ug/ml (5X) titrations	0.05 ul to 2.5 ul stock per sample
$\alpha$ - Mamma Mu 0.9 mg/ml	1 ug/ml (1X)	1.1 ul stock per sample
Pan-mouse IgG beads 4 <sup>8</sup> beads/ml (DynaL Biotech)	1 <sup>7</sup> beads/ml	125 ul stock per 5 ml volume

Blocked immunomagnetic beads were pre-washed as follows: all beads needed were pooled and washed once with 1 ml wash buffer. The beads were resuspended in a 3X volume of 1% BSA (v/v) in wash buffer and incubated for 15 min rotating at 4 °C. The beads were then washed three times with 2X volume of wash  
5 buffer and resuspended to original volume. Non-blocked beads were pooled, washed three times with 2X volume of wash buffer and resuspended to original volume.

Primary antibody was incubated with secondary beads in a fresh Eppendorf for 30 minutes, rotating at 4 °C. Approximately 200 ul wash buffer was added to increase the total volume for even mixing of the sample. The antibody-bead  
10 solution was transferred to a fresh Eppendorf, washed twice with an equal volume of wash buffer and resuspended to original volume. Target cells were added to each sample and incubated for 45 minutes, rotating at 4 °C. The tubes were transferred to a magnet, the supernatant removed, taking care not to agitate the beads, and the samples were washed twice with 1 ml wash buffer. The samples were then ready for RT-PCR  
15 using a Dynabeads mRNA direct microkit (DynaL Biotech).

Epithelial cell enrichment was placed in a magnet and supernatant was removed. The epithelial enrichment beads were then resuspended in 100 ul lysis/binding buffer fortified with Rnasin (2 U/ul per sample), and stored at -70 °C until use. Oligo (dT<sub>25</sub>) Dynabeads were pre-washed as follows: all beads needed were pooled (23  
20 ul/sample), washed three times with an excess volume of lysis/binding buffer, and resuspended to original volume. The lysis supernatant was separated with a magnet and transferred to a fresh Eppendorf. 20 ul oligo(dT<sub>25</sub>) Dynabeads were added per sample and rolled for 5 min at room temperature. Supernatant was separated using a magnet and discarded, leaving the mRNA annealed to the beads. The bead/mRNA  
25 complex was washed with buffer and resuspended in cold Tris-HCl.

For RT-PCR, the Tris-HCl supernatant was separated and discarded using MPS. For each sample containing 1<sup>5</sup> cells or less, the following was added to give a total volume of 30 ul: 14.25 ul H<sub>2</sub>O; 1.5 ul BSA; 6 ul first strand buffer; 0.75 mL 10 mM dNTP mix; 3 ul Rnasin; 3 ul 0.1M dTT; and 1.5 ul Superscript II. The resulting  
30 solution was incubated for 1 hour at 42 °C, diluted 1:5 in H<sub>2</sub>O, heated at 80°C for 2 min

to detach cDNA from the beads, and immediately placed on MPS. The supernatant containing cDNA was transferred to a new tube and stored at -20 °C.

Table IX shows the percentage of capture of P503S-transfected HEK cells as determined by RT-PCR.

5

Table IX

	% capture P503S-transfected HEK cells	% capture LnCAP cells
0.1 ug/ml P503S Mab	36.90	0.00
0.5 ug/ml P503S Mab	67.40	2.93
1 ug/ml P503S Mab	40.22	0.00
5 ug/ml P503S Mab	13.11	0.00
Anti-Mu beads only, non-blocked	1.42	0.00
Anti-Mu beads only, blocked	15.65	20.21
Absolute control, non-capture cells	100.00	100.00

10

From the foregoing it will be appreciated that, although specific embodiments of the invention have been described herein for purposes of illustration, various modifications may be made without deviating from the spirit and scope of the invention. Accordingly, the invention is not limited except as by the appended claims.

## CLAIMS

## What is Claimed:

1. An isolated polynucleotide comprising a sequence selected from the group consisting of:

(a) sequences provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942;

(b) complements of the sequences provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942;

(c) sequences consisting of at least 20 contiguous residues of a sequence provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942;

(d) sequences that hybridize to a sequence provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942 under moderately stringent conditions;

(e) sequences having at least 75% identity to a sequence of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942;

(f) sequences having at least 90% identity to a sequence of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942; and

(g) degenerate variants of a sequence provided in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591, 593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942.

2. An isolated polypeptide comprising an amino acid sequence selected from the group consisting of:

(a) sequences recited in SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-551, 553-568, 573-586, 588-590, 592, 706-708, 775, 776, 778, 780, 781, 811, 814, 818, 826, 827, 853, 855, 858, 860-862, 866-877, 879, 883-893, 895, 897, 898, 909-915, 920-928, 932-934, 940, 941 and 943;

(b) sequences having at least 70% identity to a sequence of SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-551, 553-568, 573-586, 588-590, 592, 706-708, 775, 776, 778, 780, 781, 811, 814, 818, 826, 827, 853, 855, 858, 860-862, 866-877, 879, 883-893, 895, 897, 898, 909-915, 920-928, 932-934, 940, 941 and 943;

(c) sequences having at least 90% identity to a sequence of SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-551, 553-568, 573-586, 588-590, 592, 706-708, 775, 776, 778, 780, 781, 811, 814, 818, 826, 827, 853, 855, 858, 860-862, 866-877, 879, 883-893, 895, 897, 898, 909-915, 920-928, 932-934, 940, 941 and 943;

(d) sequences encoded by a polynucleotide of claim 1;



(e) sequences having at least 70% identity to a sequence encoded by a polynucleotide of claim 1; and

(f) sequences having at least 90% identity to a sequence encoded by a polynucleotide of claim 1.

3. An expression vector comprising a polynucleotide of claim 1 operably linked to an expression control sequence.

4. A host cell transformed or transfected with an expression vector according to claim 3.

5. An isolated antibody, or antigen-binding fragment thereof, that specifically binds to a polypeptide of claim 2.

6. A method for detecting the presence of a cancer in a patient, comprising the steps of:

(a) obtaining a biological sample from the patient;  
(b) contacting the biological sample with a binding agent that binds to a polypeptide of claim 2;

(c) detecting in the sample an amount of polypeptide that binds to the binding agent; and

(d) comparing the amount of polypeptide to a predetermined cut-off value and therefrom determining the presence of a cancer in the patient.

7. A fusion protein comprising at least one polypeptide according to claim 2.

8. An oligonucleotide that hybridizes to a sequence recited in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535, 536, 552, 569-572, 587, 591,

593-606, 618-705, 709-774, 777, 789, 817, 823, 824, 878, 880-882, 894, 896, 907, 908, 916-919, 929-931, 938, 939 and 942 under moderately stringent conditions.

9. A method for stimulating and/or expanding T cells specific for a tumor protein, comprising contacting T cells with at least one component selected from the group consisting of:

- (a) polypeptides according to claim 2;
- (b) polynucleotides according to claim 1; and
- (c) antigen-presenting cells that express a polypeptide according to claim 2,

under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells.

10. An isolated T cell population, comprising T cells prepared according to the method of claim 9.

11. A composition comprising a first component selected from the group consisting of physiologically acceptable carriers and immunostimulants, and a second component selected from the group consisting of:

- (a) polypeptides according to claim 2;
- (b) polynucleotides according to claim 1;
- (c) antibodies according to claim 5;
- (d) fusion proteins according to claim 7;
- (e) T cell populations according to claim 10; and
- (f) antigen presenting cells that express a polypeptide according to claim 2.

12. A method for stimulating an immune response in a patient, comprising administering to the patient a composition of claim 11.

13. A method for the treatment of a cancer in a patient, comprising administering to the patient a composition of claim 11.

14. A method for determining the presence of a cancer in a patient, comprising the steps of:

- (a) obtaining a biological sample from the patient;
- (b) contacting the biological sample with an oligonucleotide according to claim 8;
- (c) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; and
- (d) compare the amount of polynucleotide that hybridizes to the oligonucleotide to a predetermined cut-off value, and therefrom determining the presence of the cancer in the patient.

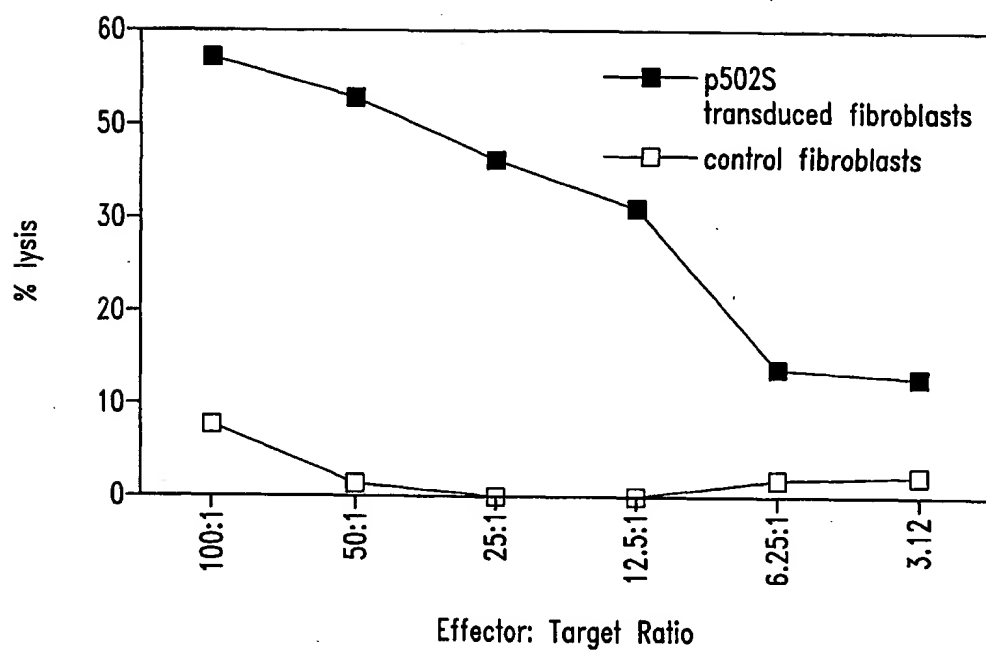
15. A diagnostic kit comprising at least one oligonucleotide according to claim 8.

16. A diagnostic kit comprising at least one antibody according to claim 5 and a detection reagent, wherein the detection reagent comprises a reporter group.

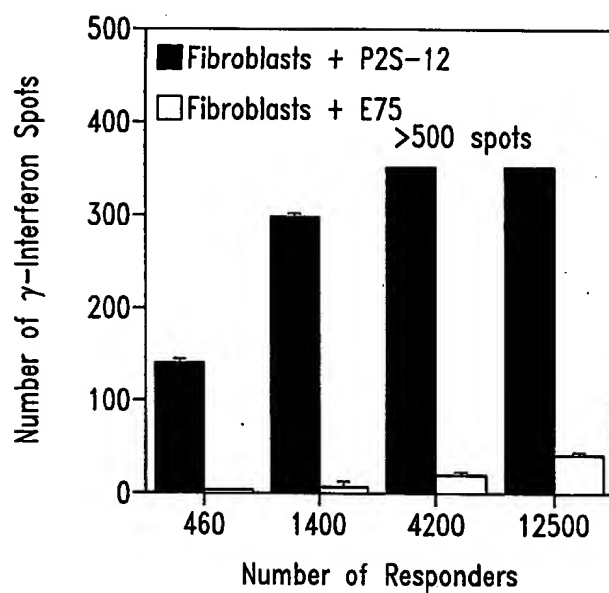
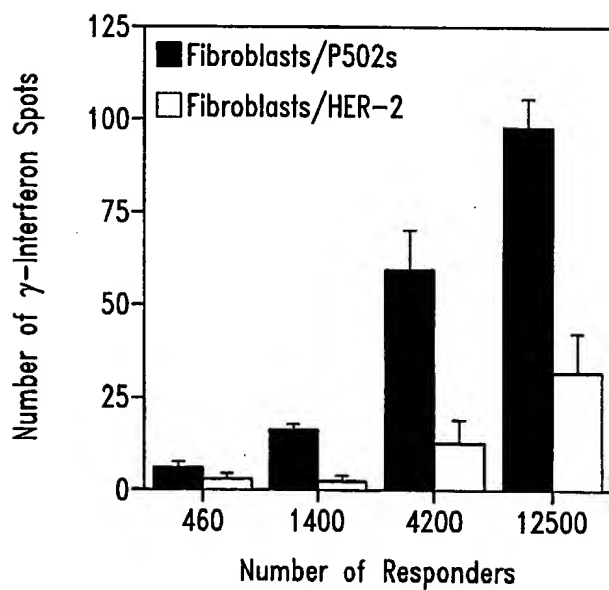
17. A method for inhibiting the development of a cancer in a patient, comprising the steps of:

- (a) incubating CD4+ and/or CD8+ T cells isolated from a patient with at least one component selected from the group consisting of: (i) polypeptides according to claim 2; (ii) polynucleotides according to claim 1; and (iii) antigen presenting cells that express a polypeptide of claim 2, such that T cell proliferate;
- (b) administering to the patient an effective amount of the proliferated T cells,  
and thereby inhibiting the development of a cancer in the patient.

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*Fig. 1*

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*Fig. 2A**Fig. 2B*

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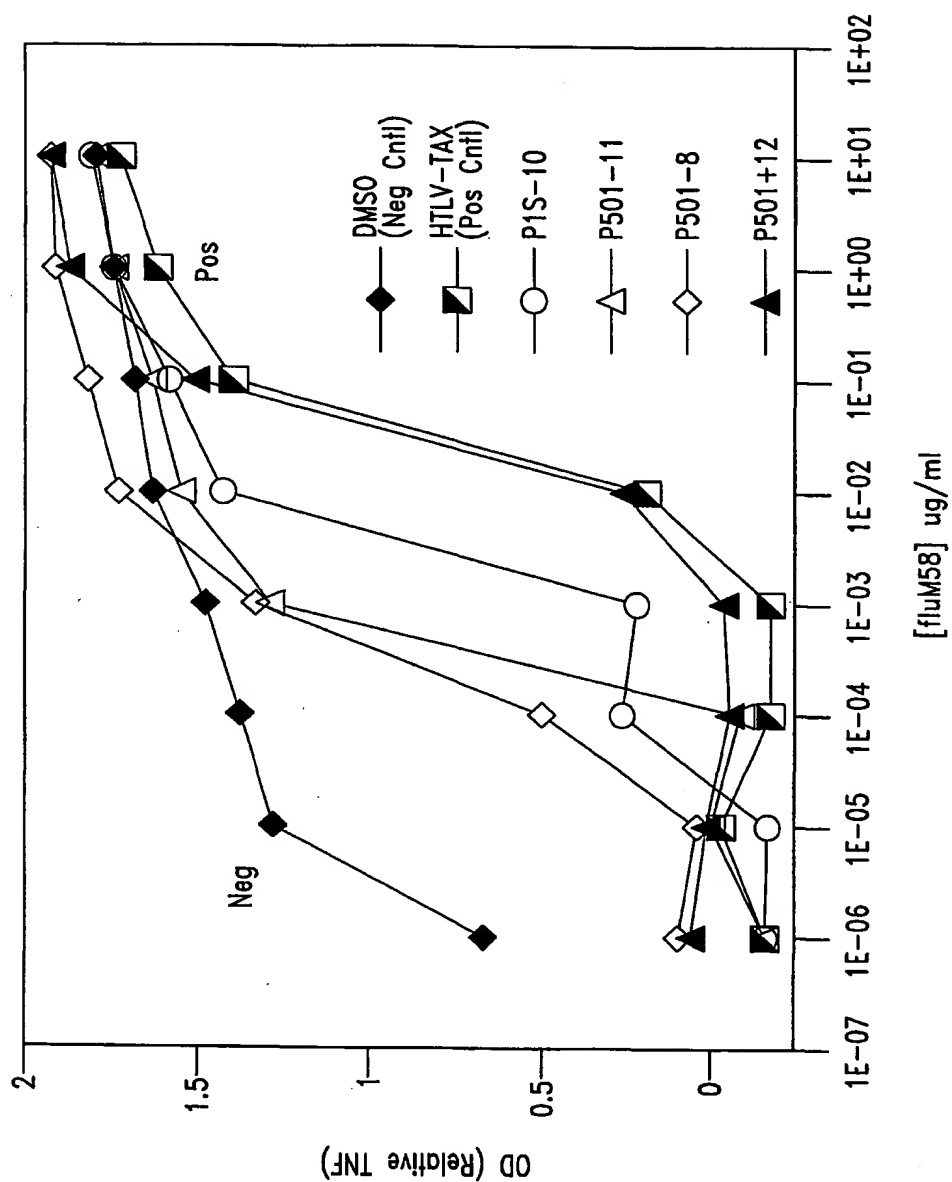
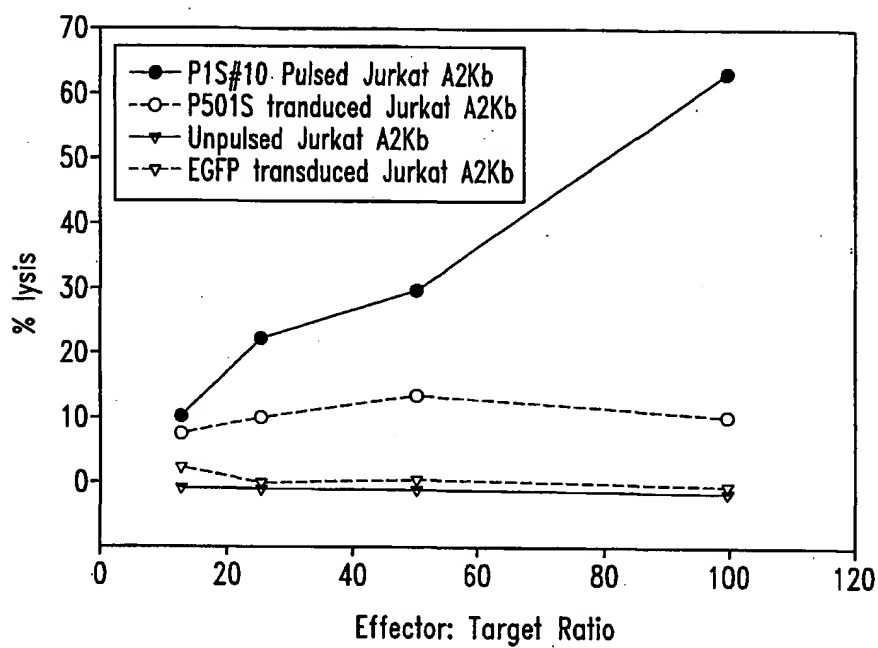
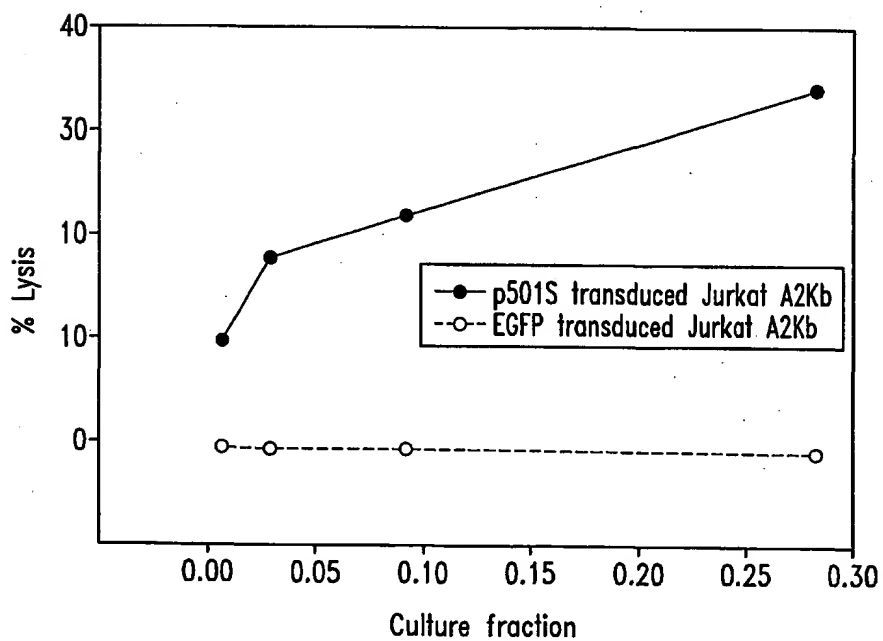
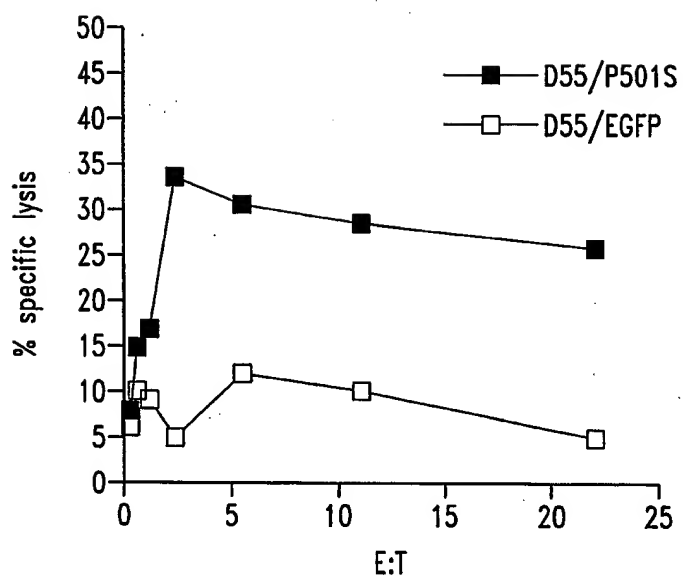
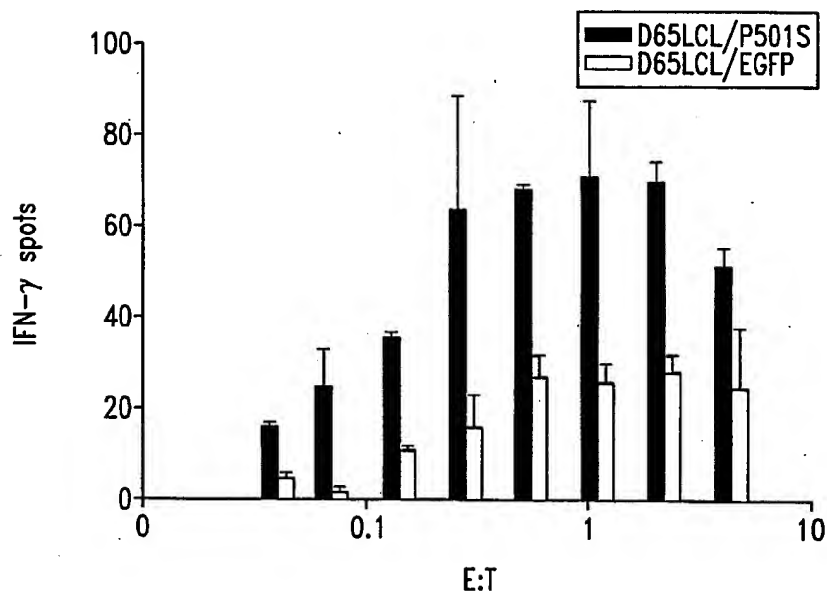


Fig. 3

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*Fig. 4**Fig. 5*

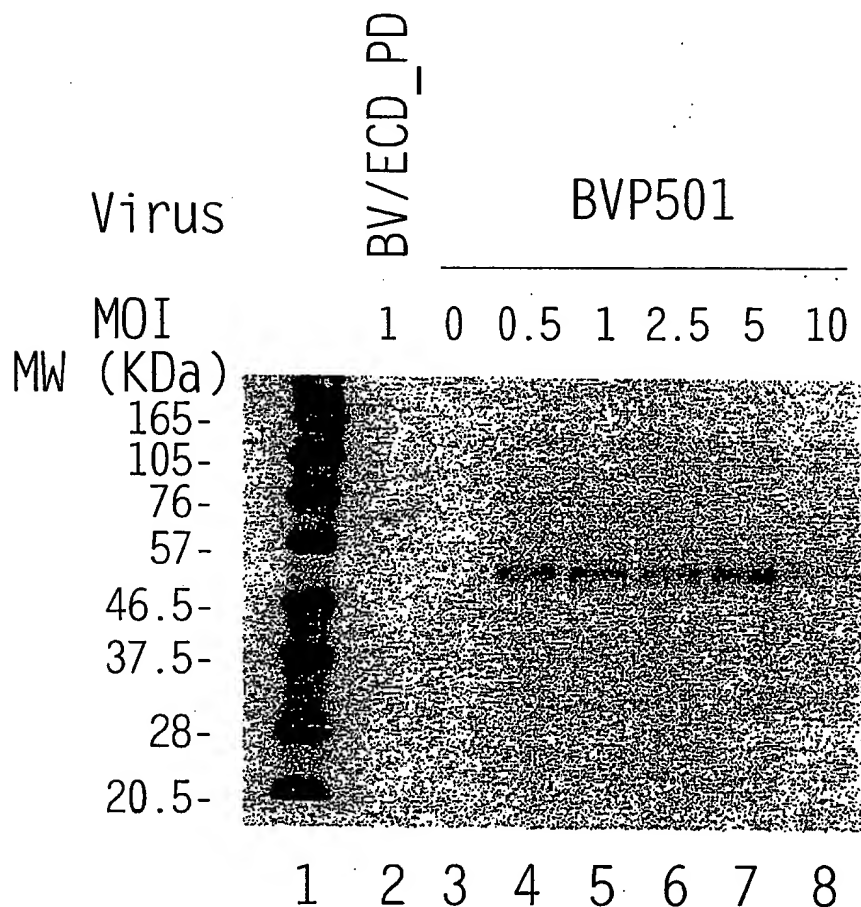
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*Fig. 6A**Fig. 6B*



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Expression of P501S  
by the Baculovirus Expression System



0.6 million high 5 cells in 6-well plate were infected with an unrelated control virus BV/ECD\_PD (lane2), without virus (lane3), or with recombinant baculovirus for P501 at different MOIs (lane 4-8). Cell lysates were run on SDS-PAGE under the reducing conditions and analyzed by Western blot with a monoclonal antibody against P501S (P501S-10E3-G4D3). Lane 1 is the biotinylated protein molecular weight marker (BioLabs).

*Fig. 7*

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FIGURE 8. Mapping of the epitope recognized by 10E3-G4-D3

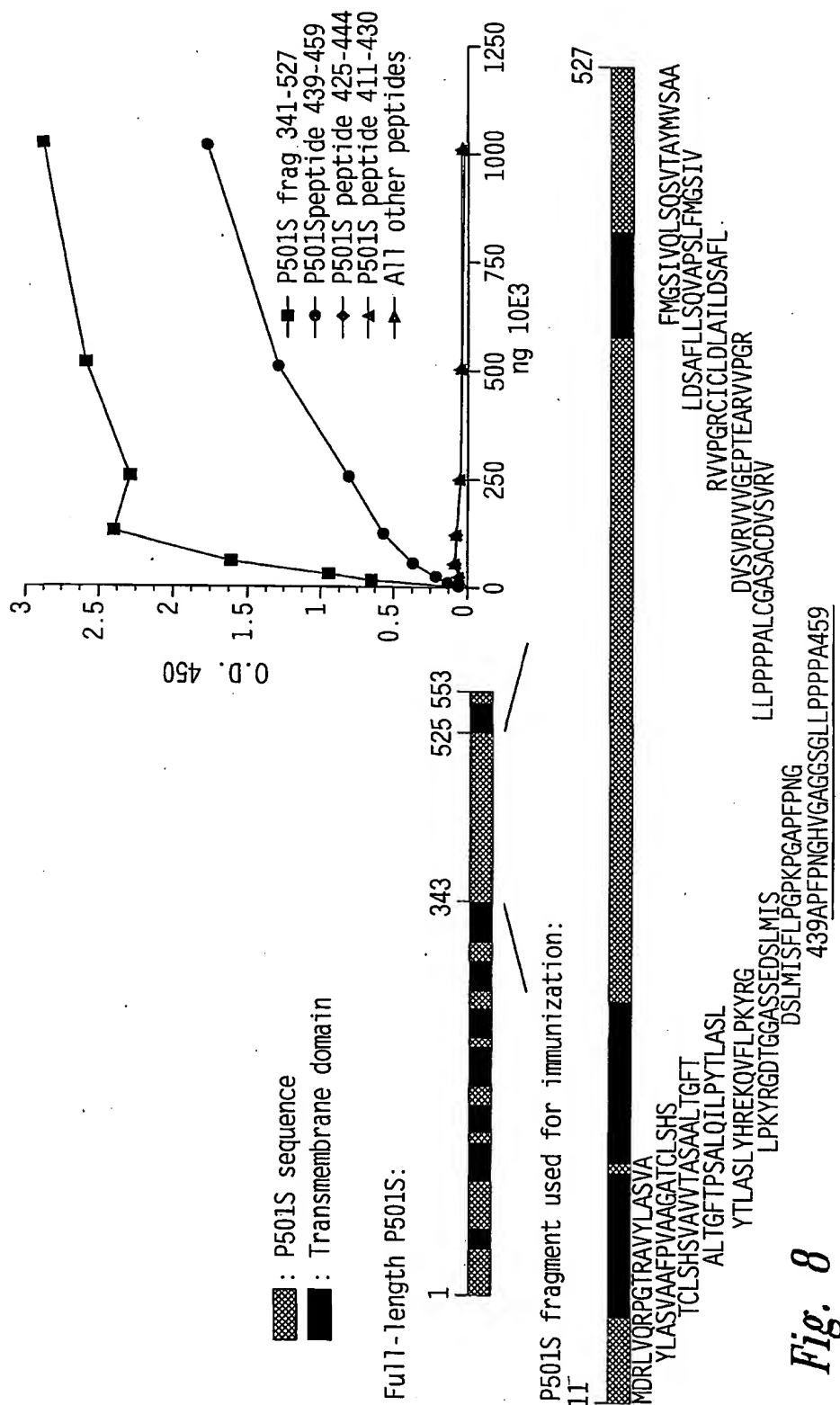


Fig. 8

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Schematic of P501S with predicted  
transmembrane, cytoplasmic, and extracellular regions

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TMVLGIGPVLGLVCYPLLGSAS

DHWRGRYGRRRP FIWALSLGILLSLFLIPRAGWL AGLLCPDPRPLE LALLILGVGLLDFCGQVCFTPL

EALLSDLFRDPDHCRQ AYSVYAFMISLGGCLGYLLPAI **DWDTSALAPYLTQEE**

CLFGLLTLIFLTCVAATLLV AEEAALGPTEPAEGLSAPSLSPHCCPCRARLAFRNLGALLPRL

HQLCCRMPTLRR LFVAELCSWMALMTFTLFYTDF **VGEGLYQGVPRAPGTEARRHYDEGVR**

MGSLGLFLQCAISLVFSLVM DRLVQRFGTRAVYLAS VAAFVPAAGATCLSHSVAVVTA **SAA**

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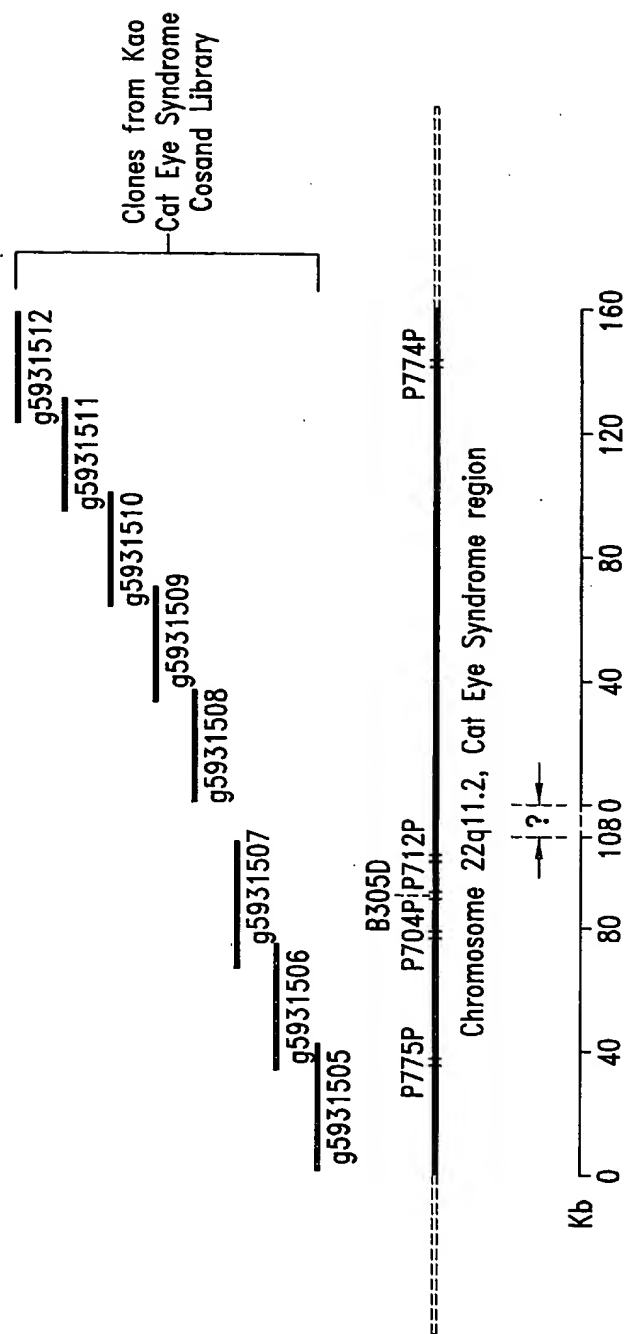
Underlined sequence: Predicted transmembrane domain; **Bold sequence**:  
 Predicted extracellular domain; *Italic sequence*: Predicted intracellular  
 domain. Sequence in bold/underlined: used generate polyclonal rabbit  
 serum

Localization of domains predicted using HMMTOP (G.E. Tusnady and I. Simon  
 (1998) Principles Governing Amino Acid Composition of Integral Membrane  
 Proteins: Applications to topology Prediction. J. Mol Biol. 283, 489-506.

*Fig. 9*

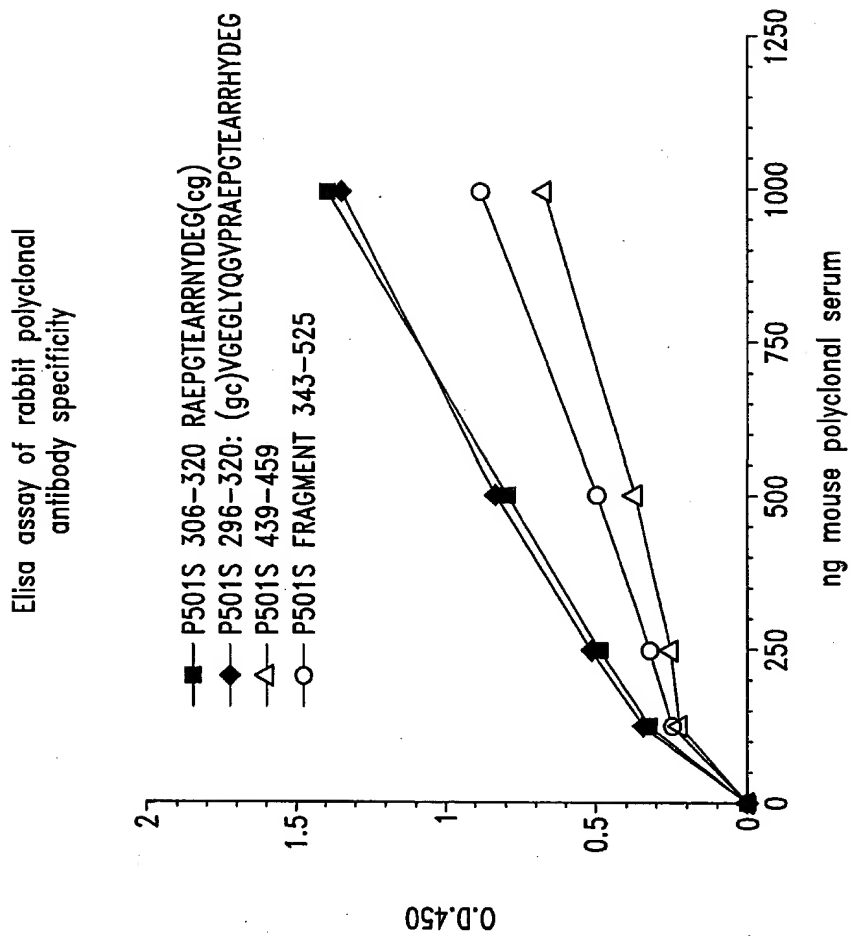
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Genomic Map of (5) Corixa Candidate Genes



*Fig. 10*

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*Fig. 11*

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*Fig. 12A (1)*

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*Fig. 12A (2)*

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*Fig. 12A (3)*



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*Fig. 12B*

## SEQUENCE LISTING

<110> Corixa Corporation  
 Xu, Jiangchun  
 Dillon, Davin C.  
 Mitcham, Jennifer L.  
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 Fanger, Gary R.  
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 Vedvick, Thomas S.  
 Carter, Darrick  
 Li, Samuel  
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 Henderson, Robert A.

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gtgactggga	aaaccctggg	cgttaccaac	ttaatcgctt	tgacgacat	ccccctttcg	540
ccagctgggc	gtaatancca	aaaggcccg	accgatcgcc	cttccaacag	ttgcgcacct	600
gaatgggnaa	atgggacccc	cctgttacgc	cgcattnaac	cccccgnggg	tttngttggt	660
acccccacnt	nnaccgctta	cactttgcc	gcgccttanc	gcccgtcccc	tttncctttt	720
cttcccttcc	tttncnccn	ctttcccccg	gggtttcccc	cntcaaacc	ona	773

<210> 4  
 <211> 828  
 <212> DNA  
 <213> Homo sapien

3

<220>  
 <221> misc\_feature  
 <222> (1)...(828)  
 <223> n = A,T,C or G

<400> 4

cctcctgagt	cctactgacc	tgtgctttct	ggtgtggagt	ccagggctgc	taggaaaagg	60
aatgggcaga	cacaggtgta	tgccaatgtt	tctgaaatgg	gtataatttc	gtcctctcct	120
tcggaacact	ggctgtctct	gaagacttct	cgctcagttt	cagtgaggac	acacacaaag	180
acgtgggtga	ccatgtttgt	tgtgggggtgc	agagatggga	gggggtgggc	ccaccctgga	240
agagtggaca	gtgacacaag	gtggacactc	tctacagatc	actgaggata	agctggagcc	300
acaatgcatg	aggcacacac	acagcaaggga	tgacnctgta	aacatagccc	acgtgtcct	360
gnnggcactg	ggaagcctan	atnaggccgt	gagcanaaag	aaggggagga	tccactagtt	420
ctanagcggc	cgccaccgcg	gtgganctcc	ancttttgtt	cccttttagtg	agggttaatt	480
gcgcgcttgg	cntaatcatg	gtcatanctn	tttctctgtg	gaaattgtta	tccgctcaca	540
attccacaca	acatacganc	cggaacata	aantgtaaac	ctgggggtgcc	taatgantga	600
ctaactcaca	ttaattgcgt	tgcgctcact	gcccgttttc	caatcnggaa	acctgtcttg	660
ccncttgcat	tnatgaatcn	gccaaacccc	ggggaaaage	gtttgcgttt	tgggcgctct	720
tccgcttctc	cnctcantta	ntccctncnc	tcggtcattc	cggctgcngc	aaaccggttc	780
accnctcca	aagggggtat	tccggtttcc	ccnaatccgg	gganance		828

<210> 5  
 <211> 834  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(834)  
 <223> n = A,T,C or G

<400> 5

tttttttttt	tttttactga	tagatggaat	ttattaagct	tttcacatgt	gatagcacat	60
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atttttatac	aatacaacac	tgtggctttt	aaaatttgg	tttcataaga	taatttatac	180
tgaagtaa	ctagccatgc	ttttaaaaa	tgcttttagt	cactccaagc	ttggcagtta	240
acatttgcca	taaaacaata	taaaacaatc	acaattta	aaataacaaa	tacaacattg	300
tagggcataa	tcatatacag	tataaggaaa	agggtgtagt	gttgagtaag	cagttattag	360
aatagaatac	cttggcctct	atgcaaata	gtctagacac	tttgattcac	tcagccctga	420
cattcagttt	tcaaagtagg	agacaggttc	tacagtatca	ttttacagtt	tccaacacat	480
tgaaaacaag	tagaaaatga	tgagttgatt	tttattaatg	cattacatcc	tcaagagtta	540
tcaccaaccc	ctcagttata	aaaaattttc	aagtatatatt	agtcataata	cttggtgtgc	600
ttattttaaa	ttagtgtctaa	atggattaag	tgaagacaac	aatggtcccc	taatgtgatt	660
gatattggtc	atttttacca	gcttcta	ctnaactttc	aggcttttga	actggaacat	720
tgnatnacag	tgttccanag	ttncaaccta	ctggaacatt	acagtgtgct	tgattcaaaa	780
tgttattttg	ttaaaaatta	aattttaacc	tggtggaaaa	ataatttgaa	atna	834

<210> 6  
 <211> 818  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(818)  
 <223> n = A,T,C or G

<400> 6

tttttttttt	tttttttttt	aagaccctca	tcaatagatg	gagacataca	gaaatagtca	60
aaccacatct	acaaaatgcc	agtatcaggc	ggcggcttcg	aagccaaagt	gatgtttgga	120
tgtaaaagtga	aatattagtt	ggcggatgaa	gcagatagtg	aggaaaagttg	agccaataat	180
gacgtgaagt	ccgtggaagc	ctgtggctac	aaaaaatgtt	gagccgtaga	tgccgtcggg	240
aatggtgaag	ggagactcga	agtactctga	ggctttagtg	agggtaaaat	agagaccag	300
taaaattgta	ataagcagtg	cttgaattat	ttggtttcgg	ttgttttcta	ttagactatg	360
gtgagctcag	gtgattgata	ctcctgatgc	gagtaatacg	gatgtgttta	ggagtgggac	420
ttctagggga	tttagcgggg	tgatgcctgt	tgggggccag	tgccctccta	gttggggggg	480
aggggctagg	ctggagtggt	aaaaggctca	gaaaaatcct	gcgaagaaaa	aaacttctga	540
ggtaataaat	aggattatcc	cgtatcgaag	gccttttttg	acaggtgggtg	tgtggtggcc	600
ttggtatgtg	ctttctcgtg	ttacatcgcg	ccatcattgg	tatatgggta	gtgtgttggg	660
ttantanggc	ctantatgaa	gaacttttgg	antggaatta	aatcaatngc	ttggccggaa	720
gtcattanga	nggctnaaaa	ggccctgtta	ngggtctggg	ctnggtttta	cccnaccat	780
ggaatncncc	ccccggacna	ntgnatccct	attcttaa			818

<210> 7  
 <211> 817  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(817)  
 <223> n = A,T,C or G

tttttttttt	tttttttttt	tggctotaga	gggggtagag	gggggtgctat	agggtaaata	60
cgggccctat	ttcaaagatt	tttaggggaa	ttaattotag	gacgatgggt	atgaaactgt	120
ggtttgctcc	acagatttca	gagcattgac	cgtagtatac	ccccggtcgt	gtagcgggtga	180
aagtgggtttg	gttttagacgt	ccgggaattg	catctgtttt	taagcctaata	gtggggacag	240
ctcatgagtg	caagacgtct	tgtgatgtaa	ttattatacn	aatgggggct	tcaatcggga	300
gtactactcg	attgtcaacg	tcaaggagtc	gcaggtcgcc	tggttctagg	aataatgggg	360
gaagtatgta	ggaattgaag	attaatccgc	cgtagtcggt	gttctcctag	gttcaatacc	420
attggtggcc	aattgatttg	atggtaaggg	gagggatcgt	tgaactcgtc	tgttatgtaa	480
aggatncctt	ngggatggga	aggcnatnaa	ggactangga	tnaatggcgg	gcangatatt	540
tcaaacngtc	tctanttcct	gaaacgtctg	aaatgttaat	aanaattaan	tttngttatt	600
gaatnttnng	gaaaagggct	tacaggacta	gaaaccaa	angaaaanta	atnntaangg	660
cnttatcntn	aaaggtgnata	accnctccta	tnatcccacc	caatngnatt	ccccacnenn	720
acnattggat	nccccanttc	canaaanggc	cnccccccg	tgnannccnc	cttttgttcc	780
cttnantgan	ggttattcnc	cctngcntt	atcance			817

<210> 8  
 <211> 799  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(799)  
 <223> n = A,T,C or G

catttccggg	tttactttct	aaggaaagcc	gagcggaagc	tgctaactgtg	ggaatcgggtg	60
cataaggaga	actttctgct	ggcacgcgct	agggacaagc	gggagagcga	ctccgagcgt	120
ctgaagcgca	cgtcccagaa	ggtggacttg	gcactgaaac	agctgggaca	catccgagag	180
tacgaacagc	gcctgaaagt	gctggagcgg	gaggtccagc	agtgtagccg	cgtcctgggg	240
tggttgccg	angcctgan	cgtctgcct	tgctgcccc	angtgggccg	ccacccctg	300
acctgcctgg	gtccaaacac	tgagccctgc	tggcggaact	caagganaac	ccccacangg	360

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ggattttgct cctanantaa ggctcatctg ggccctcgcc ccccccacctg gttggccttg 420
tctttgangt gagcccatg tccatctggg ccactgtcng gaccaccttt ngggagtgtt 480
ctccttacaa ccacannatg cccggctcct cccggaaacc antcccancc tgnagaaggat 540
caagncctgn atccactnnt nctanaaccg gccnccnccg cngtggaaacc cnccttntgt 600
tccttttctn tnagggttaa tnnccgcttg gccttnccan ngtcctnccn nttttccnnt 660
gttnaaattg ttangcncnc nccnntcccn cnnnccnccn cccgaccnccn annttnnann 720
ncctgggggt nccnncngat tgaccnccncc nccctntant tgcnttnggg nncnntgccc 780
ctttccctct nggganncg 799

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<210> 9
<211> 801
<212> DNA
<213> Homo sapien

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<220>
<221> misc_feature
<222> (1)...(801)
<223> n = A,T,C or G

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<400> 9
acgccttgat cctcccaggc tgggactggt tctgggagga gccgggcatg ctgtggtttg 60
taangatgac actcccaaag gtggtcctga cagtggccca gatggacatg gggctcacct 120
caaggacaag gccaccaggt gcggggggccg aagcccatat gatccttact ctatgagcaa 180
aatccccctgt gggggcttct ccttgaagtc cgccancagg gctcagttot tggaccocang 240
cagggtcatgg ggttgtnngc caactggggg ccncaacgca aaanggcncn gggcctcngn 300
caccocatccc angacgcggc tacactnctg gacctccnc tccaccactt tcatgcgctg 360
ttcntaccgg cgnatntgtc ccancgtgtt cngtgcncac tccancttct nggacgtgcg 420
ctacatacgc ccggantcnc nctcccgtt tgtccctatc cacgtncan caacaaattt 480
cnccntantg caccnattcc cacttttnc agntttccnc nncgngcttc cttntaaaag 540
ggttganccc cggaataatnc cccaaagggg gggggccngg tacccaactn cccctnata 600
gctgaantcc ccatnacnn gnetcnatgg anccntccnt ttaannacn ttctnaactt 660
gggaanance ctcgncntn ccccnntaa tcccncttg cnangnnct ccccnntcc 720
ncccnntng gcntntnann cnaaaaaggc ccnnancaa tctcctnnn cctcanttgc 780
ccanccctcg aaatcgccn c 801

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<210> 10
<211> 789
<212> DNA
<213> Homo sapien

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<220>
<221> misc_feature
<222> (1)...(789)
<223> n = A,T,C or G

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<400> 10
cagtctatnt ggccagtgtg gcagctttcc ctgtggctgc cgggtgccaca tgcctgtccc 60
acagtgtggc cgtggtgaca gcttcagccg ccctcaccgg gttcaccttc tcagccctgc 120
agatccctgc ctacacactg gcctccctct accaccggga gaagcaggtg ttcctgccca 180
aataccgagg ggacactgga ggtgctagca gtgaggacag cctgatgacc agcttccctg 240
caggccctaa gcctggagct ccctcccta atggacacgt ggggtgtgga ggcagtggcc 300
tgctcccacc tccaccgcg ctctgcgggg cctctgcctg tgatgtctcc gtacgtgtgg 360
tggtgggtga gccaccgan gccagggtgg ttccggggccg gggcatctgc ctggacctgc 420
ccatccctga tagtgcttc tgctgtccca ngtyggccca tccctgttta tgggtccat 480
tgtccagctc agccagtctg tcaactgcta tatggtgtct gccgcaggcc tgggtctggt 540
ccatttact ttgtacaca ggtantattt gacaagaacg anttggccaa atactcagcg 600
ttaaaaaatt ccagcaacat tgggggtgga aggctgcct cactgggtcc aactccccgc 660
tcctgttaac ccatggggc tgccggcttg gccgccatt tctgtgtctg ccaaanntat 720

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gtggctctct gctgccacct gttgctggct gaagtgcnta cngcncanct nggggggtng 780  
 gngttccc 789

<210> 11  
 <211> 772  
 <212> DNA  
 <213> Homo sapien  
 <220>  
 <221> misc\_feature  
 <222> (1)...(772)  
 <223> n = A,T,C or G

<400> 11  
 cccaccctac ccaaatatta gacaccaaca cagaaaagct agcaatggat tcccttctac 60  
 ttgtttaaat aaataagtta aatattttaa tgcctgtgtc tctgtgatgg caacagaagg 120  
 accaacaggc cacatcctga taaaaggtaa gaggggggtg gatcagcaaa aagacagtgc 180  
 tgtgggctga ggggacctgg ttcttgtgtg ttgccctca ggactcttcc cctacaaata 240  
 actttcatat gttcaaatcc catggaggag tgtttcatcc tagaaactcc catgcaagag 300  
 ctacattaaa cgaagctgca ggttaagggg cttanagatg ggaaaccagg tgactgagtt 360  
 tattcagctc ccaaaaaccc ttctctaggt gtgtctcaac taggaggcta gctgttaacc 420  
 ctgagcctgg gtaatccacc tgcagagtcc ccgcattcca gtgcatggaa cccttctggc 480  
 ctccctgtat aagtccagac tgaaccccc ttggaaggnc tccagtcagg cagccctana 540  
 aactggggaa aaaagaaaag gacgccccan cccccagctg tgcanctacg cacctcaaca 600  
 gcacagggtg gcagcaaaaa aaccacttta ctttggcaca aacaaaaact ngggggggca 660  
 accccggcac ccnangggg gttaacagga ancngggnaa cntggaacct aattnaggca 720  
 ggccnccac ccnaatntt gctgggaaat ttttctccc ctaaattntt tc 772

<210> 12  
 <211> 751  
 <212> DNA  
 <213> Homo sapien  
 <220>  
 <221> misc\_feature  
 <222> (1)...(751)  
 <223> n = A,T,C or G

<400> 12  
 gcccatttc cagctgccac accaccacag gtgactgcat tagttcggat gtcatacaaa 60  
 agctgattga agcaaccctc tacttttttg tcgtgagcct tttgcttgg gcaggtttca 120  
 ttggctgtgt tggtagctgt gtcatgcaa cagaatggg gaaaggcact gttctctttg 180  
 aagtanggtg agtctcaaaa atccgtatag ttggtgaagc cacagcactt gagcccttc 240  
 atggtggtgt tccaaacttg agtgaagtct tcctgggaac cataatcttt cttgatggca 300  
 ggcactacca gcaacgtcag ggaagtgtc agccattgtg gtgtacacca aggcgaccac 360  
 agcagctgcn acctcagcaa tgaagatgan gaggangatg aagaagaacg tcncgagggc 420  
 acacttgctc tcagtcttan caccatanca gccntgaaa accaananca aagaccacna 480  
 cnccggctgc gatgaagaaa tnacccnng ttgacaaact tgcattggcac tggganccac 540  
 agtggccnna aaaatcttca aaaaggatgc cccatcnatt gacccccaa atgcccactg 600  
 ccaacagggg ctgccccacn cncnnaacga tgancnatt gnacaagatc tncntggtct 660  
 tnatnaacnt gaaccctgcn tngtggctcc tgttcaggnc cnnggcctga cttctnaann 720  
 aangaactcn gaagncacca cngganannc g 751

<210> 13  
 <211> 729  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(729)  
 <223> n = A,T,C or G

<400> 13  
 gagccaggcg tccctctgcc tgcccactca gtggcaacac ccgggagctg ttttgcctt 60  
 tggggancct cagcagtncc ctctttcaga actcantgcc aaganccctg aacaggagcc 120  
 accatgcagt gcttcagctt cattaagacc atgatgatcc tcttcaattt gctcatcttt 180  
 ctgtgtggtg cagccctggt ggccagtggc atctgggtgt caatcgatgg ggcacccctt 240  
 ctgaagatct tcgggccact gtcgtccagt gccatgcagt ttgtcaacgt gggctacttc 300  
 ctcatcgag ccggcggtgt ggtcttagct ctaggtttcc tgggctgcta tgggtgctaag 360  
 actgagagca agtgtgccct cgtgaogtcc ttcttcatcc tccctctcat cttcattgct 420  
 gaggttgcaa tgctgtggtc gccttggtgt acaccacaat ggctgagcac ttcctgacgt 480  
 tgctggtaat gcctgccatc aanaaaagat tatgggttcc caggaaact tcaactcaagt 540  
 gttggaacac caccatgaaa gggctcaagt gctgtggctt cnnccaacta tacggatttt 600  
 gaagantcac ctacttcaaa gaaaanagt cctttccccc atttctgttg caattgacaa 660  
 acgtcccca caccagcaat tgaaccctg caccacaacc aaangggctc ccaaccanaa 720  
 attnaaggg 729

<210> 14  
 <211> 816  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(816)  
 <223> n = A,T,C or G

<400> 14  
 tgctcttctt caaagttggt cttgttgcca taacaaccac cataggtaaa gggggcgag 60  
 tgttcgtga aggggttgta gtaccagcgc gggatgctct ccttgccagag tcctgtgtct 120  
 ggcaggtcca cgcagtgcc tttgtcactg gggaaatgga tgcgctggag ctcgtcaaag 180  
 ccactcgtgt atttttcaca ggcagcctcg tccgacgcgt cggggcagtt ggggtgtct 240  
 tcacactcca ggaactgtc natgcagcag ccattgctgc agcgggaactg ggtgggctga 300  
 cangtgccag agcacactgg atggcgccct tccatgnnan gggccctgng ggaaagtccc 360  
 tganccccc anctgcctct caaangcccc acctgcaca ccccgacag ctagaatgga 420  
 atcttcttcc cgaaaggtag ttnttcttgt tgcccaancc anccccntaa acaactctt 480  
 gcanatctgc tccngggggg tcntantacc ancggtggaa aagaacccca ggcngcgaac 540  
 caancttgtt tggatncgaa gcnataatct nctnttctgc ttggtggaca gcaccantna 600  
 ctgtnnant ttagnccntg gtcctcntgg gttgnncttg aacctaatcn ccnntcaact 660  
 gggacaagg aantngccnt cctttnaatt cccnancntn cccctggtt tggggtttt 720  
 cncnctccta cccagaaaa nccgtgttcc cccccaacta ggggccnaaa ccnnttnttc 780  
 cacaaccctn cccacccac gggttcngnt ggttng 816

<210> 15  
 <211> 783  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(783)  
 <223> n = A,T,C or G

<400> 15  
 ccaaggcctg ggcaggcata nacttgaagg tacaacccca ggaaccctg gtgctgaagg 60



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atgtggaaaa cacagattgg cgcctactgc ggggtgacac ggatgtcagg gtagagagga 120
aagacccaaa ccaggtggaa ctgtggggac tcaaggaang cacctacctg ttccagctga 180
cagtgtactag ctcagaccac ccagaggaca cggccaacgt cacagtcact gtgctgtcca 240
ccaagcagac agaagactac tgccctcgcat ccaacaangt gggctcgtgc cggggctctt 300
tcccacgctg gtactatgac cccacggagc agatctgcaa gaggtttcgtt tatggaggct 360
gcttgggcaa caagaacaac taccttcggg aagaagagtg cattctancc tgtcnggggtg 420
tgcaagggtg gcctttgana ngcanctctg gggctcangc gactttcccc caggggccct 480
ccatggaaag ggcgcaccca ntgttctctg gcacctgtca gccacccag ttccgctgca 540
ncaatggctg ctgcatcnac antttcctng aattgtgaca acacccccca ntgcccccaa 600
ccctcccaac aaagcttccc tgttnaaaaa tacnccantt ggcttttnac aaacncccg 660
cncctcctt ttcccnntn aacaaagggc nctngcnttt gaactgccc n aaccnngaa 720
ctcncnngg aaaaantncc cccctgggt cctnmaance cctccncaa anctncccc 780
ccc

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&lt;210&gt; 16

&lt;211&gt; 801

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(801)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 16

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gccccaatc cagctgccac accacccacg gtgactgcat tagttcggat gtcatacaaa 60
agctgattga agcaaccctc tacttttttg tcgtgagcct tttgcttggg gcaggtttca 120
ttggctgtgt tggtagcgtt gtcattgcaa cagaatgggg gaaaggcact gttctctttg 180
aagtaggggt agtctcaaaa atccgtatag ttgggtgaagc cacagcactt gagccctttc 240
atgggtgggtg tccacacttg agtgaagtct tccctgggaac cataatcttt cttgatggca 300
ggcactacca gcaacgtcag gaagtgtca gccattgtg tgtacacca ggcgaccaca 360
gcagctgcaa cctcagcaat gaagatgagg aggaggatga agaagaacgt cncgagggca 420
cacttgctct cgtcttagc accatagcag cccangaaac caagagcaaa gaccacaacg 480
ccngctgcca atgaaagaaa ntaccacagt tgacaaactg catggccact ggacgacagt 540
tgccccgaan atcttcagaa aagggtgcc ccatcgattg aacaccana tgcccactgc 600
cnacagggct gcncncncn gaaagaatga gccattgaag aaggatcntc ntgggtctta 660
tgaactgaaa cctgcatgg tggccctgt tcagggtct tggcagtga ttctganaaa 720
aaggaacngc ntnagcccc ccaaangana aaacacccc ggggtgtgcc ctgaattggc 780
ggccaaggan cctgccccn g

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&lt;210&gt; 17

&lt;211&gt; 740

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(740)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 17

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gtgagagcca ggcgtccctc tgcccgcca ctcagtggca acacccggga gctgttttgt 60
cctttgtgga gcctcagcag ttccctcttt cagaactcac tgccaagagc cctgaacagg 120
agccaccatg cagtgtctta gtttcattaa gaccatgatg atcctcttca atttgetcat 180
ctttctgtgt ggtgcagccc tgttggcagt gggcatctgg gtgtcaatcg atggggcatc 240
ctttctgaag atcttcgggc cactgtcgtc cagtgccatg cagtttgtca acgtgggcta 300
cttcctcatc gcagccggcg ttgtgggtct tgctcttggg ttccctgggt gctatgggtc 360
taagacggag agcaaagtgt cctcgtgac gttctcttcc atcctcctcc tcattctcat 420

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tgctgaagtt gcagctgctg tggctgcctt ggtgtacacc acaatggctg aaccattcct 480
gacgttgctg gtantgcctg ccatcaanaa agattatggg tcccaggaa aaattcactc 540
aantntggaa caccnccatg aaaagggtc caatttctgn tggcttcccc aactataccg 600
gaattttgaa agantcnccc tacttccaaa aaaaaanant tgcctttnc ccenttctgt 660
tgcaatgaaa acntcccaan acngccaatn aaaacctgcc cnnncaaaaa ggntcncaa 720
caaaaaaant nnaagggttn 740

```

&lt;210&gt; 18

&lt;211&gt; 802

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(802)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 18

```

ccgctggttg cgctgggtcca gngnagccac gaagcacgtc agcatacaca gcctcaatca 60
caaggtcttc cagctgccgc acattacgca gggcaagagc ctccagcaac actgcatatg 120
ggatacactt tactttagca gccagggtga caactgagag gtgtcgaagc ttattcttct 180
gagcctctgt tagtgaggga agattccggg cttcagctaa gtagtcagcg tatgtcccat 240
aagcaaacac tgtgagcagc cggaaggtag aggcaaagtc actctcagcc agctctctaa 300
cattgggcat gtccagcagt tctccaaaca cgtagacacc agnggcctcc agcacctgat 360
ggatgagtgt ggcagcgtt gcccccttgg ccgacttggc taggagcaga aattgctcct 420
ggttctgccc tgtcaccttc acttccgcac tcatcactgc actgagtgtg ggggacttgg 480
gctcaggatg tccagagacg tggttccgcc cctcncctta atgacaccgn ccanncaacc 540
gtcggctccc gccgantgng ttogtcgtnc ctgggtcagg gtctgctggc cncacttctg 600
aancttcgtc nggcccattg aattcaccnc accggaactn gtangatcca ctnnttctat 660
aaccggncgc caccgcnntt ggaactccac tcttntncc tttacttgag ggttaaggtc 720
acccttnncc ttaccttggc ccaaacentn cctgtgtcgc anantngtna tcnggncna 780
tnccanccnc atangaagcc ng 802

```

&lt;210&gt; 19

&lt;211&gt; 731

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(731)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 19

```

cnaagcttcc aggtnacggg ccgcnaance tgaccnagg tancanaang cagnncggg 60
gagcccaccg tcacgnggng gngtctttat nggagggggc ggagccacat cnetggacnt 120
cntgacccca actcccncc ncnantgca gtgatgagt cagaactgaa ggtnacgtg 180
caggaaccaa gancaaannc tgctccnntc caagtcggcn nagggggcgg ggctggccac 240
gencatcct cnagtgtcgn aaagcccn cctgtctact tgtttggaga acngcnnga 300
catgcccagn gttanataac nggcnagag tnannttggc tctcccttcc ggctgcgcan 360
cngtntgtc tagnggacat aacctgacta cttaactgaa cccnngaate tncnccct 420
ccactaagct cagaacaaaa aacttcgaca ccactcantt gtcacctgnc tgctcaagta 480
aagtgtaccc catncccaat gntgtcng ngtctgnc tgcnttangt tcggtcctgg 540
gaagacctat caattnaagc tatgtttctg actgcctctt gctccctgna acaancnacc 600
cnnnntcca aggggggnc ggccccaat cccccaacc ntnaattnan tttancccn 660
ccccnggcc cggccttcta cnancntcnn nnaacgggna aaacnnngc tttncccaac 720
nnaatccncc t 731

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10

<210> 20  
 <211> 754  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(754)  
 <223> n = A,T,C or G

<400> 20  
 tttttttttt tttttttttt taaaaacccc ctccattnaa tgnaaacttc cgaaattgtc 60  
 caaccccctc ntccaaatnn cntttccgg gngggggttc caaacccaan ttanntttgg 120  
 annttaaatt aaatnttntt tggngggnna anccnaatgt nangaaagtt naaccanta 180  
 tnancttnaa tncctggaaa cngtngntt ccaaaaatnt ttaaccctta antccctccg 240  
 aaatngttna nggaaaaccc aanttctcnt aaggttggtt gaaggntnaa tnaaaanccc 300  
 nnccaattgt ttttngccac gcctgaatta attggnntcc gntgttttcc nttaaaanaa 360  
 ggnnancccc ggttantnaa tcccccnnc cccaattata ccganttttt ttingaattgg 420  
 gancccnccg gaattaacgg ggnnntccc tnttgggggg cnggnncccc ccccntcggg 480  
 ggttngggnc aggnncnaat tgtttaagg tccgaaaaat ccctccnaga aaaaaanctc 540  
 ccaggntgag nntnggggtt ncccccccc canggccct ctcgnanagt tggggtttgg 600  
 ggggcctggg atttntttc cctnttnc tcccccccc cngggganag aggttngngt 660  
 tttgntcncn ggcncncn aaganctttn ccganttnan ttaaatccnt gcctnggcga 720  
 agtcnttgn agggntaaan ggccccctnn cggg 754

<210> 21  
 <211> 755  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(755)  
 <223> n = A,T,C or G

<400> 21  
 atcancat gacccnaac nngggaccnc tcancggnc nnnnacnc cggccnatca 60  
 nngtnagnnc actncnntn natcacnccc cncnactac gccncnanc cnacgcnta 120  
 nncanatncc actganngcg cgangtngan ngagaaanct nataccanag ncaccanacn 180  
 ccagctgtcc nanaangcct nnnatacngg nnnatccaat ntgnancctc cnaagtattn 240  
 nncnncanat gattttctn anccgattac cntncccc tanccctcc cccccaacna 300  
 cgaaggcnct ggnccnaagg nngcgnccc ccgctagntc cccnncagt cncncncta 360  
 aactcancn nattacncgc ttctgagta tcaactcccc aatctaccc tactcaactc 420  
 aaaaaanacn gatacaaaat aatncaagcc tgnttatnac actntgactg ggtctctatt 480  
 ttagnggtcc ntnaancntc ctaatactc cagtctnct tcnccaattt ccnaangget 540  
 ctttcngaca gcatntttt gttcccnntt gggttcttan ngaattgcc ttcntngaac 600  
 gggtctctct tttccttcgg ttancctggg ttcnccggc cagttattat tttccntttt 660  
 aaattcctnc cntttanttt tggcnttca aaccccggc cttgaaaacg gcccctggt 720  
 aaaaggttgt tttganaaaa ttttgtttt gttcc 755

<210> 22  
 <211> 849  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(849)

<223> n = A,T,C or G

<400> 22

tttttttttt	tttttangtg	tngtcgtgca	ggtagaggct	tactacaant	gtgaanacgt	60
acgctnggan	taangcgacc	cganttctag	ganncnccct	aaaatcanac	tgtgaagatn	120
atcctgnnna	cggaanggtc	accggnggat	nntgctaggg	tgncnctcc	cannncnttn	180
cataactcng	nggccctgcc	caccaccttc	ggcggcccng	ngnccgggcc	cgggtcattn	240
gnnttaaccn	cactnngcna	ncggtttccn	nccccnnng	accnnggcga	tccggggtn	300
tctgtcttcc	cctgnagncn	anaaantggg	ccnccgnccc	ctttaccct	nnacaagcca	360
cngccntcta	ncnccngccc	ccccctccant	nngggggact	gccnanngt	ccgttncctng	420
nnaccccnnn	gggtncctcg	gttgtcgant	cnaccgnang	ccanggattc	cnaaggaagg	480
tgcgttnttg	gcccctaccc	ttcgtcncgg	nncacccctc	ccgacnanga	nccgctcccg	540
cncnncgng	cctcncctcg	caacacccgc	nctctcngt	ncggnnnccc	ccccaccgc	600
ncctcncnc	ngnccgnancn	ctcncncnc	gtctcannca	ccaccccgcc	ccgccaggcc	660
ntcanccacn	ggnggacnng	nagcncntc	gcncgcgcgn	gcgncnccct	cgccncngaa	720
ctnctcngg	ccantnncgc	tcaancnna	cnaaacgcgc	ctgcgcggcc	cgnagcgncc	780
ncctcncga	gtcctcccg	cttcnacc	angnnttcn	cgaggacacn	nnaccccgcc	840
nncangcgg						849

<210> 23

<211> 872

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(872)

<223> n = A,T,C or G

<400> 23

gcgcaacta	tacttcgctc	gnactcgtgc	gcctcgtcnc	tcttttctc	cgcaaccatg	60
tctgacnanc	ccgattnggc	ngatatacn	aagntcganc	agtccaaact	gantaacaca	120
cacacnncn	aganaaatcc	nctgccttcc	anagtanacn	attgaacnng	agaaccangc	180
nggggaatcg	taatnaggcg	tgcgcgcga	atntgtcnc	gtttatttn	ccagctcnc	240
ctnccnacc	tactcttcn	nagctgtcnn	accctcngtn	cgnaccccc	naggtcggga	300
tccgggtttn	nntgaccgng	cnnccctcc	ccccctccat	nacganccnc	ccgcaccacc	360
nanngcncg	nccccgnct	cttcgcnc	ctgtcctntn	ccccgtngc	ctggcncngn	420
accgcattga	ccctcgccnn	ctnccngaaa	ncgnanacgt	ccgggttgn	annancgctg	480
tgggnnngcg	tctgcncgc	gttccttcn	ncncttcca	ccatcttct	tacnnggtct	540
ccnccctc	tcnnncacnc	cctgggacgc	tntcctntgc	cccccttnac	tccccctct	600
cgncgtgncc	cgccccacc	ntcatttnca	nacgntcttc	acaannncct	ggtnnctcc	660
cnancngncn	gtcanccnag	ggaaggngg	ggnnccnntg	nttgacgttg	nggngangtc	720
cgaanantcc	tcnccntcan	cctaccct	cgggcgnct	ctcngttnc	aacttancaa	780
ntctccccg	ngngcncntc	tcagcctcnc	ccncccnct	ctctgcantg	tntctgctc	840
tnaccnntac	gantnttcgn	cncctcttt	cc			872

<210> 24

<211> 815

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(815)

<223> n = A,T,C or G

<400> 24

gcatgcaagc	ttgagtattc	tatagngtca	cctaaatanc	ttggcntaat	catggtcnta	60
------------	------------	------------	------------	------------	------------	----

nctgnccttc	tgtgtcaaat	gtatacnaa	tanatatgaa	tctnatntga	caagannnga	120
tcntncatta	gtaacaantg	tnntgtccat	cctgtcnngan	canattccca	tnnattncgn	180
cgcattcnen	gcncantatn	taatngggaa	ntcnntnnn	ncaccnncat	ctatcntncc	240
gcnccttgac	tgganagat	ggatnanttc	tnntntgacc	nacatgttca	tcttggattn	300
aanancccc	cgcngnccac	cgggtngnng	cnagccnntc	ccaagacctc	ctgtggaggt	360
aacctgcgtc	aganncatca	aacntgggaa	acccgcnncc	angtnnaagt	ngnnncanan	420
gatcccgctc	aggnttnacc	atcccttcnc	agcgccccct	ttngtgcctt	anagnnagc	480
gtgtccnanc	cncctcaacat	ganacgcgcc	agnccanccg	caattnggca	caatgtcgnc	540
gaaccccta	gggggantna	tncaaanccc	caggattgtc	cncncangaa	atcccnanc	600
ccnccctac	ccncttttg	gacngtgacc	aantcccgga	gtncacagtc	ggccngnctc	660
ccccaccggt	nncntgggg	gggtgaanct	cngnntcanc	cngncgaggn	ntcgnaagga	720
accggnctn	ggncgaanng	ancnntcnga	agngccnct	cgtataaccc	cccctcncca	780
nccnacngnt	agntcccccc	cngggtnccg	aangg			815

&lt;210&gt; 25

&lt;211&gt; 775

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(775)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 25

ccgagatgtc	tcgctccgtg	gccttagctg	tgctcgcgt	actctctctt	tctggcctgg	60
aggctatcca	gcgtactcca	aagattcagg	tttactcacg	tcattccagca	gagaatggaa	120
agtcaaattt	cctgaattgc	tatgtgtctg	ggtttcatcc	atccgacatt	gaanttgact	180
tactgaagaa	tgganagaga	attgaaaaag	tggagcattc	agacttgctt	ttcagcaagg	240
actggctctt	ctatctontg	tactacactg	aattcacccc	cactgaaaaa	gatgagtatg	300
cctgccgtgt	gaaccatgtg	actttgtcac	agcccaagat	agttaagtgg	gatcgagaca	360
tgtaagcagn	cnncatggaa	gtttgaagat	gccgcatttg	gattggatga	attccaaatt	420
ctgcttgctt	gcnttttaat	antgatatgc	ntatacaccc	taccctttat	gncccccatt	480
tgtaggggtt	acatnantgt	tcnctntnga	catgatcttc	ctttataant	ccnccnttgc	540
aattgcccgt	cnccngttn	ngaattgttc	cnnaaccacg	gttggctccc	ccaggtcncc	600
tcttacggaa	gggcctgggc	cnccttncaa	ggttggggga	accnaaaatt	tcnctntgc	660
ccncccncca	cnntcttgng	nncncanttt	ggaacccttc	cnattcccct	tggcctcnaa	720
nccttnncta	anaaaacttn	aaancgtngc	naaannttn	acttcccccc	ttacc	775

&lt;210&gt; 26

&lt;211&gt; 820

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(820)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 26

anattantac	agtgtaatct	tttcccagag	gtgtgtanag	ggaacggggc	ctagaggcat	60
cccanagata	ncttatanca	acagtgcctt	gaccaagagc	tgctgggcac	atttcctgca	120
gaaaagggtg	cggtoceccat	cactctcct	ctcccatagc	catcccagag	gggtgagtag	180
ccatcangcc	ttcgggtggga	gggagtcang	gaaacaacan	accacagagc	anacagacca	240
ntgatgacca	tgggcgggag	cgagcctctt	ccctgnaccg	gggtggcana	nganagccta	300
netgaggggt	cacactataa	acgttaacga	ccnagatnan	cacctgcctc	aagtgcaccc	360
ttctacctg	acnaccagng	accnnnaact	gcngcctggg	gacagcnctg	ggancagcta	420
acnnagcact	cacctgcccc	cccatggcgc	tnccgntccc	tggtcctgnc	aagggaagct	480

```

ccctgttgga attncgggga naccaaggga nccccctcct ccanctgtga aggaaaaann 540
gatggaattt tncctttccg gccnntcccc tcttcttita cagccccct nntactcnc 600
tccctctntt ntctgtncnc acttttnacc cennnatctt ccttnattga tcggannctn 660
ganattccac tnnccctnc cctcncatng naanacnaaa nactntctna cccnggggat 720
gggnccctcg ntcatcctct ctttttctct accnccnntt ctttgctct ccttngatca 780
tccaaacntc gntggccntn cccccccnnn tcttttcccc 820

```

&lt;210&gt; 27

&lt;211&gt; 818

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(818)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 27

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tctgggtgat ggcctcttcc tctcaggga cctctgactg ctctgggcca aagaatctct 60
tgtttcttct ccgagcccca ggcagcgggtg attcagccct gcccaacctg attctgatga 120
ctgcgggatgc tgtgacggac ccaaggggca aatagggtcc cagggtccag ggagggcgcg 180
ctgctgagca ctcccgcccc tcacctgcc cagccctgc catgagctct gggctgggtc 240
tccgcctcca gggttctgct ctccangca ngccancaag tggcgctggg ccacactggc 300
ttcttctgct cccctccctg gctctganc tctgtcttcc tgtcctgtgc angcnccttg 360
gatctcagtt tccctcncctc anngaactct gttctgann tcttcantta actntgantt 420
tatnaacnan tggnetgtnc tgtcnnactt taatgggccc gaccggctaa tccctccctc 480
nctcccttcc antcnnnna accngcttnc cctcctctcc centancccg ccnggggaanc 540
ctcctttgcc ctnaccangg gccnnnaccg cccntnnctn ggggggcnng gtnnctnenc 600
ctgntnnccc cncctcncnt tncctcgtcc cnnncnccn ngcannntc ncngtcccn 660
tnnctcttct ngntcgnaa ngntcncntn tnnnnngncc ngntnntncc tccctctcnc 720
cnnntgnang tnnntnnnnc ncngnncccc nnnnnnnnn nggnntnnnn tctnccnccg 780
cccnccccc ngnattaagg cctccnntct ccggccnc 818

```

&lt;210&gt; 28

&lt;211&gt; 731

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(731)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 28

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aggaagggcg gagggatatt gtanggggatt gagggatagg agnataangg gggaggtgtg 60
tcccaacatg anggtgnngt tctcttttga angaggggtg ngtttttann ccnggtgggt 120
gattnaaccc cattgtatgg agnnaaagg ttttagggat ttttcggctc ttatcagtat 180
ntanattcct gtnaatcgga aaatnatntt tcnnccngaa aatnttgctc ccatccgnaa 240
attnctcccg ggtagtgcatt nttngggggn cngccangtt tcccaggctg ctanaatcgt 300
actaaagntt naagtgggan tncaaatgaa aacctnncac agagnatccn tacccgactg 360
tnnnntnctt tcgccctntg actctgcnnng agcccaatac ccnngngnat gtcncccnng 420
nnngcgnccn tgaannnnnc tcgnggctnn gancatcang ggggttcgca tcaaaagcnn 480
cgtttcccat naaggcactt tngcctcctc caaccnctng cctcnncca tttngccgtc 540
nggttcnctt acgctnntng cncctnnntn ganattttnc ccgcctnggg naancctcct 600
gnaatgggta gggnccttntc ttttnaccnn gnggtntact aatcnnctnc acgcntnctt 660
tctcnacccc cccctttttt caatcccanc ggcnaatggg gtctcccncc cgangggggg 720
nnnccannnc c 731

```

14

<210> 29  
 <211> 822  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(822)  
 <223> n = A,T,C or G

<400> 29  
 actagtccag tgtggtggaa ttccattgtg ttgggggncnc ttctatgant antnttagat 60  
 cgctcanacc tcacancctc cncacnangc ctataangaa nannaataga nctgtncnnt 120  
 atntntacnc tcatanncct cnnnaccac tccctcttaa cccntactgt gcctatngcn 180  
 tnnctantct ntgccgectn cnanccacn gtggggcnc cncnngnatt ctcnatctcc 240  
 tcnccatntn gcctananta ngtnccatacc ctatacctac nccaatgcta nnnctaancn 300  
 tccatnantt annntaacta ccaactgacnt ngactttcnc atnancctct aatttgaatc 360  
 tactctgact cccacngcct annnattagc ancntcccc nacnatntct caaccaaadc 420  
 ntcaacaacc tatctantctg ttcnccaacc nttncctccg atccccnnac aacccccctc 480  
 ccaaataccc nccacctgac ncctaaccn caccatcccg gcaagccnan ggnccatttan 540  
 ccactggaat cacnatngga naaaaaaac ccnaactctc tancncnnat ctccctaana 600  
 aatnctcctn naatttactn ncantnccat caanccacn tgaaacnnaa cccctgtttt 660  
 tanatccctt ctttcgaaaa ccnaccctt annncccaac ctttngggcc ccccnctnc 720  
 ccnaatgaag gncncccaat cnangaaacg nccttgaaaa ancnaaggcna anannntccg 780  
 canatcctat cccttanttn ggggnccctt ncccnngggc cc 822

<210> 30  
 <211> 787  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(787)  
 <223> n = A,T,C or G

<400> 30  
 cgcccgctg ctctggcaca tgcctcctga atggcatcaa aagtgatgga ctgcccattg 60  
 ctagagaaga ccttctctcc tactgtcatt atggagccct gcagactgag ggtccccctt 120  
 gtctgcagga tttgatgtct gaagtcgtgg agtgtggctt ggagctcctc atctacatna 180  
 gctggaagcc ctggagggcc tctctcgcca gctccccct tctctccacg ctctccangg 240  
 acaccagggg ctccaggcag cccattattc ccagnangac atggtgtttc tccacgcgga 300  
 cccatggggc ctgnaaggcc agggctcctt ttgacaccat ctctcccgtc ctgctggga 360  
 ggccgtggga tccactantt ctanaacggn cggcaccng gtgggagctc cagcttttgt 420  
 tccnttaat gaaggttaat tgcncgcttg gcgtaatcat nggtcanaac tnttctctgt 480  
 gtgaaattgt ttntccctc ncnattccnc ncnacatacn aaccgggaan cataaagtgt 540  
 taaagcctgg gggtnccctn nngaattnaac tnaactcaat taattgcgtt ggctcatggc 600  
 ccgctttccn ttcnngaaaa ctgtntccc ctgcnttntt gaatcgcca cccccnggg 660  
 aaaagcgggt tgcnttttng ggggntcctt ccncttccc cctcnctaan cctnccgct 720  
 cggtcgttnc nggtngcggg gaangggnat nnnctccnc naaggggng agnnngntat 780  
 ccccaaa 787

<210> 31  
 <211> 799  
 <212> DNA  
 <213> Homo sapien

<220>

<221> misc\_feature  
 <222> (1)...(799)  
 <223> n = A,T,C or G

<400> 31  
 tttttttttt ttttttttggc gatgctactg ttttaattgca ggaggtgggg gtgtgtgtac 60  
 catgtaccag ggctattaga agcaagaagg aaggaggagg ggcagagcgc cctgctgagc 120  
 aacaaaggac tcctgcagcc ttctctgtct gtctcttggc gcaggcacat ggggaggcct 180  
 cccgcagggt gggggccacc agtccagggt tgggagcact acannggggtg ggagtgggtg 240  
 gtggctggtn cnaatggcct gncacanatc cctacgattc ttgacacctg gatttcacca 300  
 ggggaccttc tgttctcca nggnaacttc nttnatctcn aaagaacaca actgtttctt 360  
 cngcanttct ggctgttcat ggaaagcaca ggtgtccnat ttnggctggg acttgggtaca 420  
 tatggttccg gccacctct cccntcnaaa aagtaattca ccccccccn cctctnttg 480  
 cctgggcccct taantaccca caccggaact canttantta ttcatcttng gntgggcttg 540  
 ntnatncnn cctgaangcg ccaagttgaa aggccacgcc gtnccnctc cccatagnan 600  
 nttnnnct canctaagc cccccnggc aacnatccaa tcccccccn tgggggcccc 660  
 agcccanggc ccccgctcg ggnnnccngn cncgnantcc ccaggnctc ccantcngnc 720  
 ccnnngcncc cccgcacgca gaacanaagg ntngagcnc cgcannnnnn nggtnnncac 780  
 ctgcccccc cenncgng 799

<210> 32  
 <211> 789  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(789)  
 <223> n = A,T,C or G

<400> 32  
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 ttttnccnag ggcagggtta ttgacaacct cncgggacac aancaggctg gggacaggac 120  
 ggcaacaggc tccggcgggc gggcgggcgc cctacctgc ggtacaaaat ntgcagcctc 180  
 cgctcccgct tgatnttct ctgcagctgc aggatgccnt aaaaacaggc ctcggccntn 240  
 ggtgggcacc ctgggatttn aatttccacg ggcacaatgc ggtcgcancc cctcaccacc 300  
 nattaggaat agtggtnnta cccnccnccg ttggcncact ccccntggaa accacttntc 360  
 gcggtccgg catctggtct taaaccttgc aaacnctggg gccctctttt tggttantnt 420  
 nccngccaca atcatnact agactggcnc gggctggccc caaaaaancn ccccaaaacc 480  
 ggncatgtc tttnccgggt tgctgcnatn tncatcacct cccgggcnc naaggncaac 540  
 ccaaaagtct ttngggcccn caaaaaanct cgggggggnc ccagtttcaa caaagtcac 600  
 ccccttgccc cccaaatcct cccccgntt nctgggtttg ggaaccacg cctctnnctt 660  
 tggnnngcaa gntggntccc ccttcggggc cccggtgggc ccnctctaa ngaaaacncc 720  
 ntccctnnca ccatcccc nngnnacgnc tancaangna tccctttttt tanaaacggg 780  
 cccccnccg 799

<210> 33  
 <211> 793  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(793)  
 <223> n = A,T,C or G

<400> 33  
 gacagaacat gttggatggt ggagcacctt tctatacgac ttacaggaca gcagatggg 60



16

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aattcatggc tgttgagca atanaacccc agttctacga gctgctgac aaaggacttg 120
gactaaagtc tgatgaactt cccaatcaga tgagcatgga tgattggcca gaaatgaana 180
agaagtttgc agatgtattt gcaaagaaga cgaaggcaga gtggtgtcaa atctttgacg 240
gcacagatgc ctgtgtgact ccggttctga cttttgagga ggttgttcat catgatcaca 300
acaangaacg gggctcgttt atcaccantg aggagcagga cgtgagcccc cgccctgcac 360
ctctgctgtt aaacacccca gccatccctt ctttcaaaag ggatccacta cttctagagc 420
ggncgccacc gcggtggagc tccagctttt gttcccttta gtgagggtta attgcgcgt 480
tggcgtaatc atggtcatan ctgtttcctg tgtgaaattg ttatccgctc acaattccac 540
acaacatacg anccggaagc atnaaatttt aaagcctggn ggtngcctaa tgantgaact 600
nactcacatt aattggcttt gcgctcactg cccgctttcc agtccggaaa acctgtcctt 660
gccagctgcc nttaatgaat cnggccaccc cccggggaaa aggcngtttg cttnttgggg 720
cgcncttccc gctttctcgc ttctgaant ccttcccccc ggtctttcgg cttgcggcna 780
acggtatcna cct 793

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&lt;210&gt; 34

&lt;211&gt; 756

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(756)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 34

```

gccgcgaccg gcatgtacga gcaactcaag ggcgagtggg accgtaaaag ccccaatctt 60
ancaagtgcg gggaaanagct gggctcgactc aagctagttc ttctggagct caacttcttg 120
ccaaccacag ggaccaagct gaccaaacag cagctaattc tggcccgatga catactggag 180
atcggggccc aatggagcat cctacgcaan gacatcccct ccttcgagcg ctacatggcc 240
cagctcaaat. gctactactt tgattacaan gagcagctcc ccgagtcagc ctatatgcac 300
cagctcttgg gcctcaacct cctcttcctg ctgtcccaga accgggtggc tgantnccac 360
acgganttgg ancggtctgcc tgcccanga catacanacc aatgtctaca tcnaccacca 420
gtgtcctgga gcaatactga tgganggcag ctaccncaa gtnttccttg ccnagggtaa 480
catccccgcg cgagagctac accttcttca ttgacatcct gctcgacact atcagggatg 540
aaaatcgcn ggttgctcca gaaaggctnc aanaanatcc ttttcnctga aggcccccgg 600
atnncntagt nctagaatcg gcccgccatc gcggtgganc ctccaacctt tcggttccct 660
ttactgaggg ttnattgcg cccttggcgt tatcatggte acnccngttn cctgtgttga 720
aatntntaac cccccacaat tccacgccna cattnng 756

```

&lt;210&gt; 35

&lt;211&gt; 834

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(834)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 35

```

gggatctct anatonacct gnatgcattg ttgtcgggtg ggtcgtctgc gatgaanatg 60
aacaggatct tgcccttgaa gctctcggct gctgtnttta agttgctcag tctgccgtca 120
tagtcagaca cncctcttgg caaaaaacan caggatntga gtcttgattt cacctccaat 180
aatcttcngg gctgtctgct ccgtgaactc gatgacnang ggcagctggt tgtgtntgat 240
aaantccanc angttctcct tggtagctc cccttcaaag ttgttccggc cttcatcaaa 300
cttctnnaan angannancc canctttgtc gagctggnat ttgganaaca cgtcactggt 360
ggaaactgat cccaaatggt atgtcatcca tcgcctctgc tgctgcaaa aaacttgctt 420
ggcncaaata cgactcccn tccttgaaag aagcncatca caccocctc octggactcc 480

```

17

```

nncaangact ctncgcgtnc cccntccnng cagggttggt ggcannccgg gcccntgcgc 540
ttcttcagcc agttcacnat nttcatcagc ccctctgcc gctgtntat tccttggggg 600
ggaanccgtc tctcccttcc tgaannaact ttgaccgtng gaatagccgc gcntcncnt 660
acntnctggg cggggttcaa antccctccn ttgncnntcn cctcgggcca ttctggattt 720
nccnaacttt ttccttcccc cncccnccgg ngtttggnnt tttcatnggg ccccaactct 780
gctnttggcc antccctgg gggcntntan cnccccctnt ggtcccntng ggc 834

```

&lt;210&gt; 36

&lt;211&gt; 814

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(814)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 36

```

cggncgcttt ccngcgcgc cccgtttcca tgaacnaaggc tcccttcang ttaaatacnn 60
cctagnaaac attaatgggt tgctctacta atacatcata cnaaccagta agcctgcca 120
naacgccaac tcaggccatt cctaccaaag gaagaaaggc tggctctctc acccctgta 180
ggaaaggcct gccttgtaag acaccacaat ncggctgaat ctnaagtctt gtgttttact 240
aatggaaaaa aaaaaataaac aanagggtttt gttctcatgg ctgccaccg cagcctggca 300
ctaaaacanc ccagcgctca cttctgcttg ganaaatatt ctttgcctt ttggacatca 360
ggcttgatgg tatcactgcc acntttccac ccagctgggc ncccttccc catntttgtc 420
antganctgg aaggcctgaa ncttagtctc caaaagtctc ngcccacaag accggccacc 480
aggggagtc nttncagtg gatctgcaa anantaccn tatcatcnnt gaataaaaag 540
gccctgaac ganatgcttc cancanctt taagacccat aatcctngaa ccatggtgcc 600
cttcgggtct gatccnaaag gaatgttctt gggteccant cctcctttg ttncctacgt 660
tgtnttggaac ccntgctngn atnaccnaan tganatcccc ngaagcacc tnccttggc 720
atgtganttt cntaaattct ctgccctacn nctgaaagca cnattccctn ggcncnaan 780
ggngaactca agaaggtctn ngaaaaacca cncn 814

```

&lt;210&gt; 37

&lt;211&gt; 760

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(760)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 37

```

gcatgctgct cttcctcaaa gttgttcttg ttgccataac aaccaccata ggtaaagcgg 60
gcgcagtgtt cgctgaagg gttgtagtac cagcgcgga tgctctcct gcagagtcct 120
gtgtctggca ggtccacgca atgcccttg tctctggga aatggatgcg ctggagctcg 180
tcnaanccac tcgtgtattt ttcacangca gcctcctccg aagcntccgg gcagttggg 240
gtgtcgtcac actccactaa actgtcgatn cancagccca ttgctgcagc ggaactgggt 300
gggtgacag gtgccagaac aactggatn ggcctttcca tggaaagggc tgggggaaat 360
cncctnancc caaactgcct ctcaaaggcc accttgaca ccccgacagg ctagaaatgc 420
actcttcttc ccaaaggtag ttgttcttgt tgcccaagca ncctccanca aacccaaaanc 480
ttgcaaaaatc tgctccgtgg ggtcatnnn taccanggtt ggggaaanaa acccggcngn 540
ganccnctt gtttgaatgc naaggnaata atcctcctgt cttgcttggg tggaanagca 600
caattgaact gttaaanttg ggccgngtt cncnnggtg gtctgaaact aatcaccgtc 660
actggaaaaa ggtangtgcc ttccttgaat tcccaaannt cccctngntt tgggtntttt 720
ctcctctncc ctaaaaatcg tnttcccccc centanggcg 760

```

<210> 38  
 <211> 724  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(724)  
 <223> n = A,T,C or G

<400> 38  
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 cttccnaaat tgtccaaccc cctcnnccaa atnnccattt cggggggggg gttccaaacc 120  
 caaattaatt ttgganttta aattaaatnt tnattngggg aanaanccaa atgtnaagaa 180  
 aatttaaccc attatnaact taaatncctn gaaacccttg gnttccaaaa atttttaacc 240  
 cttaaattccc tccgaaattg ntaanggaaa accaaattcn cctaaggctn ttggaagggt 300  
 ngatttaaac ccccttnant tnttttnacc cnnngctnaa ntatttngnt tccggtgttt 360  
 tcctnttaan cntnggtaac tcccgnataat gaannncctt aanccaatta aaccgaattt 420  
 tttttgaatt ggaaattccn ngggaattna cgggggtttt tcccttttg gggccatncc 480  
 cccnctttcg ggggtttggg ntaggttgaa tttttnnang ncccaaaaaa ncccccaana 540  
 aaaaaactcc caagnnttaa ttngaattnc ccccttccca ggccttttg gaaaggnggg 600  
 tttntggggg ccngggantt cnttccccn ttncncccc ccccccnggt aaanggttat 660  
 ngnttttgtt ttttgggcc cttnanggac cttccggatn gaaattaaat ccccggnccg 720  
 gccg 724

<210> 39  
 <211> 751  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(751)  
 <223> n = A,T,C or G

<400> 39  
 tttttttttt tttttctttg ctcacattta atttttattt tgattttttt taatgctgca 60  
 caacacaata tttatttcat ttgtttcttt tatttccattt tatttggttg ctgctgctgt 120  
 tttatttatt tttactgaaa gtgagaggga acttttgttg ccttttttcc tttttctgta 180  
 ggccgcctta agctttctaa atttggaaaca tctaagcaag ctgaanggaa aagggggttt 240  
 cgcaaatca ctcgggggaa nggaaagggt gctttgttaa tcatgcccta tgggtgggtga 300  
 ttaactgctt gtacaattac ntttcaactt taattaattg tgctnaangc ttaattana 360  
 cttgggggtt cctccccan accaacccon ctgacaaaaa gtgcngccc tcaaatnatg 420  
 tcccgcnnt cnttgaaaca cacngcngaa ngttctcatt ntcccnnc caggtnaaaa 480  
 tgaagggtta ccatntttaa cnccacctcc acntggcnnn gcctgaatcc tcnaaaan 540  
 ccctcaanen aatnctnng ccccggtcnc gcntnngtcc cnccggtt cggggaantn 600  
 cccccnga anncnntnnc naacnaaatt ccgaaaatat tcccnntcnc tcaattcccc 660  
 cnnagactnt cctcnncnan cncaatttcc ttttnntcac gaacnngnnc cnnaaatgn 720  
 nnnncnctc cncnngtccn naatcnccan c 751

<210> 40  
 <211> 753  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(753)

<223> n = A, T, C or G

<400> 40

gtgggtatttt	ctgtaagatc	aggtgttcct	ccctcgtagg	tttagaggaa	acaccctcat	60
agatgaaaac	ccccccgaga	cagcagcact	gcaactgcc	agcagccggg	gtaggagggg	120
cgccctatgc	acagctgggc	ccttgagaca	gcagggttc	gatgtcaggc	tcgatgtcaa	180
tggtctggaa	gcggcggctg	tacgtgcgta	ggggcacacc	gtcaggggcc	accaggaact	240
tctcaaagtt	ccaggcaacn	tcgttgcgac	acaccggaga	ccagggtgatn	agcttggggg	300
cggtcataa	cgcggtggcg	tcgtcgctgg	gagctggcag	ggcctcccgc	aggaaggcna	360
ataaaagggtg	cgcccccgca	ccgttcantc	cgcacttctc	naanaccatg	angttgggct	420
cnaaccocacc	accannccgg	acttccttga	nggaattccc	aaatctcttc	gntcttgggc	480
ttctnctgat	gccctanctg	gttgcccngn	atgccaanca	nccccaancc	ccgggggtcct	540
aaanaccccn	cctcctcntt	tcactctggg	tnttntcccc	ggaccntggg	tcctctcaag	600
ggancccata	tctcnaccan	tactcacent	nccccccent	gnnaccanc	cttctanngn	660
ttccncccg	ncctctggcc	cntcaaan	gcttnacna	cctgggtctg	ccttcccccc	720
tnccctatct	gnaccccn	ttgtctcan	tnt			753

<210> 41

<211> 341

<212> DNA

<213> Homo sapien

<400> 41

actatatcca	tcacaacaga	catgcttcat	cccatagact	tcttgacata	gottcfaatg	60
agtgaaccca	tccttgattt	atatacatat	atgttctcag	tattttggga	gcctttccac	120
ttcttttaac	cttgttcatt	atgaacactg	aaaataggaa	tttgtgaaga	gttaaaaagt	180
tatagcttgt	ttacgtagta	agtttttgaa	gtctacattc	aatccagaca	cttagttgag	240
tgttaaactg	tgatttttaa	aaaatatcat	ttgagaatat	tctttcagag	gtattttcat	300
ttttactttt	tgatttaattg	tgttttatat	attagggtag	t		341

<210> 42

<211> 101

<212> DNA

<213> Homo sapien

<400> 42

acttaactgaa	tttagttctg	tgctcttcct	tatttagtgt	tgtatcataa	atactttgat	60
gtttcaaaca	ttctaaataa	ataattttca	gtggcttcat	a		101

<210> 43

<211> 305

<212> DNA

<213> Homo sapien

<400> 43

acatctttgt	tacagtctaa	gatgtgttct	taaataacca	ttccttcctg	gtcctcaccc	60
tccaggggtg	tctcacactg	taattagagc	tattgaggag	tctttacagc	aaattaagat	120
tcagatgcct	tgctaagtct	agagttctag	agttatgttt	cagaaaagtct	aagaaaccca	180
cctcttgaga	ggtcagtaaa	gaggacttaa	tatttcatat	ctacaaaatg	accacaggat	240
tggtacacaga	acgagagtta	tcctggataa	ctcagagctg	agtacctgcc	cgggggccgc	300
tcgaa						305

<210> 44

<211> 852

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature  
 <222> (1)...(852)  
 <223> n = A,T,C or G

<400> 44  
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 gattatttgg tgtgtgtttt ggtttgtgtc caaagtattg gcagcttcag ttttcatttt 120  
 ctctccatcc tcgggcattc ttcccaaatt tatataccag tcttcgtcca tccacacgct 180  
 ccagaatttc tctttttag tagtatctca tagctcggct gagcttttca taggtcatgc 240  
 tgctgttgtt cttcttttta ccccatagct gagccactgc ctctgatttc aagaacctga 300  
 agacgccctc agatcgggtc tcccatttta ttaatcctgg gttcttgtct gggttcaaga 360  
 ggatgtcgcg tagtaattcc cataagttag tccctctcgg gttgtgcttt ttgggtgtggc 420  
 acttggcagg ggggtcttgc tcttttttca tatcagggtga ctctgcaaca ggaagggtgac 480  
 tgggtggtgt catggagatc tgagcccgcc agaaagtatt gctgtccaac aaatctactg 540  
 tgctaccata gttgtgttca tataaatagt tctngtcttt ccagggtgtt atgatggaag 600  
 gctcagtttg ttcagtcttg acaatgacat tgtgtgtgga ctggaacagg tcactactgc 660  
 actggccgtt ccacttcaga tgctgcaagt tgctgtagag gagnetgccc gccgtccctg 720  
 ccgcccgggt gaactcctgc aaactcatgc tgcaaagggt ctgcgcgttg atgtcgaact 780  
 cntggaaagg gatcaattg gcatccagct ggttgggtgc caggaggtga tggagccact 840  
 cccacacctg gt 852

<210> 45  
 <211> 234  
 <212> DNA  
 <213> Homo sapien

<400> 45  
 acaacagacc cttgtcgcgt aacgacctca tgctcatcaa gttggacgaa tccgtgtccg 60  
 agtctgacac catccggagc atcagcattg cttcgcagtg cctaccgcg gggaactctt 120  
 gcctcgtttc tggctggggt ctgctggcga acggcagaat gctaccgtg ctgcagtgcg 180  
 tgaacgtgtc ggtgtgtctt gaggaggtct gcagtaagct ctatgaccgc ctgt 234

<210> 46  
 <211> 590  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(590)  
 <223> n = A,T,C or G

<400> 46  
 actttttatt taaatgttta taaggcagat ctatgagaat gatagaaaac atgggtgtgta 60  
 atttgatagc aatatttttg agattacaga gttttagtaa ttaccaatta cacagttaaa 120  
 aagaagataa tatattccaa gcanatacaa aatatctaata gaaagatcaa ggcaggaaaa 180  
 tgantataac taattgacaa tggaaaatca attttaatgt gaattgcaca ttatccttta 240  
 aaagctttca aaanaaanaa ttattgcagt ctanttaatt caaacagtgt taaatggtat 300  
 caggataaan aactgaaggc canaaagaat taattttcac ttcattgtaac ncacccanatt 360  
 ttacaatggc ttaaatgcan ggaaaaagca gtggaagtag ggaagtantc aaggctcttc 420  
 tggctctctaa tctgccttac tctttgggtg tggctttgat cctctggaga cagctgccag 480  
 ggctcctgtt atatccacaa tcccagcagc aagatgaagg gatgaaaaag gacacatgct 540  
 gccttccttt gagagactt catctcactg gccaacactc agtcacatgt 590

<210> 47  
 <211> 774  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(774)  
 <223> n = A,T,C or G

<400> 47  
 acaagggggc ataatgaagg agtgggggana gatttttaaag aaggaaaaaa aacgaggccc 60  
 tgaacagaat ttctctgnac aacgggggctt caaaataatt ttcttgggga ggttcaagac 120  
 gcttcaactgc ttgaaactta aatggatgtg ggacanaatt ttctgtaatg accctgaggg 180  
 cattacagac gggactctgg gaggaaggat aaacagaaaag gggacaaaag ctaatcccaa 240  
 aacatcaaag aaaggaagggt ggcgtcatac ctcccagcct acacagttct ccagggtctt 300  
 cctcatccct ggaggacgac agtggaggaa caactgacca tgtcccagg ctcctgtgtg 360  
 ctggctcctg gtcttcagcc cccagctctg gaagcccacc ctctgctgat cctgcgtggc 420  
 ccacactcct tgaacacaca tccccagggt atattcctgg acatggctga acctcctatt 480  
 cctacttcog agatgccttg ctccctgcag cctgtcaaaa tcccactcac cctccaaacc 540  
 acggcatggg aagcctttct gacttgccctg attactocag catcttgga caatccctga 600  
 ttccccactc cttagaggca agataggggt gttaagagta gggctggacc acttgaggcc 660  
 aggtgtctgg cttcaaattt tggctcattt acgagctatg ggaccttggg caagtnatct 720  
 tcacttctat gggcctcatt ttgttctacc tgcaaaatgg gggataataa tagt 774

<210> 48  
 <211> 124  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(124)  
 <223> n = A,T,C or G

<400> 48  
 canaaattga aattttataa aaaggcattt ttctcttata tccataaaat gatataattt 60  
 ttgcaantat anaaatgtgt cataaattat aatgttcctt aattacagct caacgcaact 120  
 tgggt 124

<210> 49  
 <211> 147  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(147)  
 <223> n = A,T,C or G

<400> 49  
 gccgatgcta ctattttatt gcaggagggtg ggggtgtttt tattattctc tcaacagctt 60  
 tgtggctaca ggtgggtgtct gactgcatna aaaanttttt tacgggtgat tgcaaaaatt 120  
 ttagggcacc catatcccaa gcantgt 147

<210> 50  
 <211> 107  
 <212> DNA  
 <213> Homo sapien

<400> 50  
 acattaaatt aataaaagga ctgttggggt tctgctaaaa cacatggctt gatatatgtc 60

atggtttgag gttaggagga gttaggcata tgttttgga gaggggt 107

<210> 51  
 <211> 204  
 <212> DNA  
 <213> Homo sapien

<400> 51  
 gtccaggaa gtctaggga cacacgactc tggggtcacg gggccgacac acttgacgg 60  
 cgggaaggaa aggcagagaa gtgacaccgt cagggggaaa tgacagaaag gaaaatcaag 120  
 gccttgcaag gtcagaaagg ggactcaggg cttccaccac agccctgcc cacttgccca 180  
 cctccctttt gggaccagca atgt 204

<210> 52  
 <211> 491  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(491)  
 <223> n = A,T,C or G

<400> 52  
 acaagataa catttatctt ataacaaaaa tttgatagtt ttaaagggtta gtattgtgta 60  
 ggtatttttc caaaagacta aagagataac tcaggtaaaa agttagaaat gtataaaaca 120  
 ccatcagaca ggtttttaaa aaacaacata ttacaaaatt agacaatcat ccttaaaaaa 180  
 aaaacttctt gtatcaattt cttttgttca aaatgactga cttaantatt tttaaatatt 240  
 tcanaaacac ttctcaaaaa attttcaana tggtagcttt canatgtnc ctcagtccca 300  
 atgttgctca gataaataaa tctcgtgaga acttaccacc caccacaagc tttctggggc 360  
 atgcaacagt gtcttttctt tnccttttct tttttttttt ttacaggcac agaaactcat 420  
 caattttatt tggataacaa agggctctca aattatattg aaaaataaat ccaagttaat 480  
 atcactcttg t 491

<210> 53  
 <211> 484  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(484)  
 <223> n = A,T,C or G

<400> 53  
 acataattta gcagggctaa ttaccataag atgctattta ttaanaggtn tatgatctga 60  
 gtattaacag ttgctgaagt ttggtatttt tatgcagcat tttctttttg ctttgataac 120  
 actacagaac ccttaaggac actgaaaatt agtaagtaaa gttcagaaac attagctgct 180  
 caatcaaact tctacataac actatagtaa ttaaaacgtt aaaaaaaagt gttgaaatct 240  
 gactagtat anaccgctcc tgtcaggata anactgcttt ggaacagaaa gggaaaaanc 300  
 agctttgant ttctttgtgc tgatangagg aaaggctgaa ttaccttgtt gcctctccct 360  
 aatgattggc aggtcnggta aatnccaaaa catattccaa ctcaacactt ctttccncc 420  
 tancctgant ctgtgtattc caggancagg cggatggaat gggccagccc ncggatgttc 480  
 cant 484

<210> 54  
 <211> 151  
 <212> DNA

<213> Homo sapien

<400> 54

actaaacctc gtgcttgtga actccatata gaaaacgggtg ccatccctga acacggctgg	60
ccactgggta tactgctgac aaccgcaaca acaaaaacac aaatccttgg cactggctag	120
tctatgtcct ctcaagtgcc tttttgtttg t	151

<210> 55

<211> 91

<212> DNA

<213> Homo sapien

<400> 55

acctggcttg tctccgggtg gttcccggcg cccccacgg tccccagaac ggacactttc	60
gccctccagt ggatactga gccaaagtgg t	91

<210> 56

<211> 133

<212> DNA

<213> Homo sapien

<400> 56

ggcggatgtg cggttggttat atacaaatat gtcattttat gtaagggact tgagtatact	60
tggatttttg gtatctgtgg gttgggggga cgggccagga accaataccc catggatacc	120
aagggacaac tgt	133

<210> 57

<211> 147

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(147)

<223> n = A,T,C or G

<400> 57

actctggaga acctgagccg ctgctccgcc tctgggatga ggtgatgcan gcngtggcgc	60
gactgggagc tgagcccttc cctttgcgcc tgcctcagag gattgttgcc gacntgcana	120
tctcantggg ctggatncat gcagggt	147

<210> 58

<211> 198

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(198)

<223> n = A,T,C or G

<400> 58

acagggatat aggtttnaag ttattgtat tgtaaaatac attgaatttt ctgtatactc	60
tgattacata catttatcct ttaaaaaaga tgtaaatcctt aatttttatg ccatctatta	120
atttaccat gatgtacctt gtaaatgaga agtcatgata gactgaatt ttaactagtt	180
ttgacttcta agtttgggt	198

<210> 59



<211> 330  
 <212> DNA  
 <213> Homo sapien

<400> 59  
 acaacaaatg ggttgtagg aagtcttata agcaaaactg gtgatggcta ctgaaaagat 60  
 ccattgaaaa ttatcattaa tgatttttaa tgacaagtta tcaaaaactc actcaatttt 120  
 cacctgtgct agcttgctaa aatgggagtt aactctagag caaatatagt atcttctgaa 180  
 tacagtcaat aaatgacaaa gccaggcct acaggtggtt tccagacttt ccagaccag 240  
 cagaaggaat ctattttatc acatggatct cgtctgtgc tcaaaatacc taatgatatt 300  
 ttcgtcttt attggacttc ttgaagagt 330

<210> 60  
 <211> 175  
 <212> DNA  
 <213> Homo sapien

<400> 60  
 accgtgggtg ccttctacat tcttgacggc tcttcacca acatctggtt ctacttcggc 60  
 gtctgggtg ccttctctt catctcctc cagctggtgc tgctcatcga ctttgcgcac 120  
 tcttggaacc agcgtgggt gggcaaggcc gaggagtgcg attcccgtgc ctggt 175

<210> 61  
 <211> 154  
 <212> DNA  
 <213> Homo sapien

<400> 61  
 accccacttt tctcctgtg agcagtctgg acttctcact gctacatgat gagggtagt 60  
 ggttggtgct cttcaacagt atcctccct ttccggatct gctgagccg acagcagtgc 120  
 tggactgcac agccccggg ctccacattg ctgt 154

<210> 62  
 <211> 30  
 <212> DNA  
 <213> Homo sapien

<400> 62  
 cgctcgagcc ctatagttag tcgtattaga 30

<210> 63  
 <211> 89  
 <212> DNA  
 <213> Homo sapien

<400> 63  
 acaagtcatt tcagaccct ttgctcttca aaactgacca tcttttatat ttaatgcttc 60  
 ctgtatgaat aaaaatggtt atgtcaagt 89

<210> 64  
 <211> 97  
 <212> DNA  
 <213> Homo sapien

<400> 64  
 accggagtaa ctgagtcggg acgctgaatc tgaatccacc aataaataaa ggttctgcag 60  
 aatcagtga tccaggattg gtccttggat ctggggt 97

<210> 65  
 <211> 377  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(377)  
 <223> n = A,T,C or G

<400> 65  
 acaacaanaa ntcccttctt taggccactg atggaaacct ggaacccctt ttgatggca 60  
 gcatggcgct ctaggccttg acacagcggc tggggtttgg gctntcccaa accgcacacc 120  
 ccaaccctgg tctacccaca nttctggcta tgggctgtct ctgccactga acatcagggg 180  
 tcggtcataa natgaaatcc caanggggac agaggtcagt agaggaagct caatgagaaa 240  
 ggtgctgttt gctcagccag aaaacagctg cctggcattc gccgctgaac tatgaaccg 300  
 tgggggtgaa ctacccccc gaggaatcat gcctggcgga tgcaanggtg ccaacaggag 360  
 gggcgggagg agcatgt 377

<210> 66  
 <211> 305  
 <212> DNA  
 <213> Homo sapien

<400> 66  
 acgcctttcc ctcagaattc agggaagaga ctgtcgctg ccttcctccg ttgttgctg 60  
 agaaccctg tgccccttcc caccatatcc accctcgctc catctttgaa ctcaaacacg 120  
 aggaactaac tgcaccctgg tcctctcccc agtccccagt tcaccctcca tcctcacct 180  
 tcctccactc taagggatat caacactgcc cagcacaggg gccctgaatt tatgtggtt 240  
 ttatatattt tttataaaga tgcactttat gtcatttttt aataaagtct gaagaattac 300  
 tgttt 305

<210> 67  
 <211> 385  
 <212> DNA  
 <213> Homo sapien

<400> 67  
 actacacaca ctccacttgc ccttgtgaga cactttgtcc cagcacttta ggaatgctga 60  
 ggtcggacca gccacatctc atgtgcaaga ttgccagca gacatcaggt ctgagagttc 120  
 ccctttttaa aaaggggact tgcttaaaaa agaagtctag ccacgattgt gtagagcagc 180  
 tgtgtgtgtc tggagattca cttttgagag agttctcctc tgagacctga tctttagagg 240  
 ctgggcagtc ttgcacatga gatggggctg gtctgatctc agcactcctt agtctgcttg 300  
 cctctcccag ggccccagcc tggccacacc tgcttacagg gcactctcag atgccatac 360  
 catagtttct gtgctagtgg accgt 385

<210> 68  
 <211> 73  
 <212> DNA  
 <213> Homo sapien

<400> 68  
 acttaaccag atatattttt accccagatg gggatattct ttgtaaaaaa tgaaaataaa 60  
 gtttttttaa tgg 73

<210> 69  
 <211> 536  
 <212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(536)

<223> n = A,T,C or G

<400> 69

actagtccag	tgtggtggaa	ttccattgtg	ttgggggctc	tcaccctcct	ctcctgcagc	60
tccagctttg	tgctctgcct	ctgaggagac	catggcccag	catctgagta	ccctgctgct	120
cctgctggcc	accctagctg	tggccctggc	ctggagcccc	aaggaggagg	ataggataat	180
cccgggtggc	atctataacg	cagacctcaa	tgatgagtgg	gtacagcgty	cccttcactt	240
cgccatcagc	gagtataaca	aggccaccaa	agatgactac	tacagacgty	cgctgcgggt	300
actaagagcc	aggcaacaga	ccgttggggg	ggtgaattac	ttcttcgacg	tagaggtggg	360
ccgaaccata	tgtaccaagt	cccagcccaa	cttgacaccc	tgtyccttcc	atgaacagcc	420
agaactgcag	aagaacacgt	tgtgctcttt	cgagatctac	gaagttccct	ggggagaaca	480
gaangtcctt	gggtgaaatc	caggtgtcaa	gaaatccctan	ggatctgttg	ccaggc	536

<210> 70

<211> 477

<212> DNA

<213> Homo sapien

<400> 70

atgaccctta	acagggggcc	tctcagccct	cctaattgacc	tccggcctag	ccatgtgatt	60
tcactttccac	tccataacgc	tcctcatact	aggcctacta	accaacacac	taaccatata	120
ccaatgatgg	cgcgatgtaa	cacgagaaag	cacataccaa	ggccaccaca	caccacctgt	180
ccaaaaaggc	cttcgatacg	ggataatcct	atttattacc	tcagaagttt	ttttcttgcg	240
agggattttt	ctgagccttt	taccactcca	gcctagcccc	taccccccaa	ctaggagggc	300
actggccccc	aacaggcatc	accccgctaa	atcccctaga	agtcccactc	ctaaacacat	360
ccgtattact	cgcatcagga	gtatcaatca	cctgagctca	ccatagtcta	atagaaaaca	420
accgaaacca	aattattcaa	agcactgctt	attacaattt	tactgggtct	ctattttt	477

<210> 71

<211> 533

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(533)

<223> n = A,T,C or G

<400> 71

agagctatag	gtacagtgtg	atctcagctt	tgcaaacaca	ttttctacat	agatagtact	60
aggtattaat	agatatgtaa	agaaagaaat	cacaccatta	ataatggtaa	gattgggttta	120
tgtgatttta	gtggtatttt	tggcaccctt	atatatgttt	tccaaacttt	cagcagtgat	180
attattttcca	taacttaaaa	agtgagtttg	aaaaagaaaa	tctccagcaa	gcattctcatt	240
taaataaaagg	tttgtcatct	ttaaaaatac	agcaatatgt	gactttttta	aaaagctgtc	300
aaataggtgt	gaccctacta	ataattatta	gaaatacatt	taaaaacatc	gagtacotca	360
agtcagtttg	ccttgaaaaa	tatcaaatat	aactcttaga	gaaatgtaca	taaaagaatg	420
cttcgtaatt	ttggagtang	aggttccctc	ctcaattttg	tatttttaaa	aagtacatgg	480
taaaaaaaaa	aattcacaa	agtatataag	gctgtaaaat	gaagaattct	gcc	533

<210> 72

<211> 511

<212> DNA

<213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(511)  
 <223> n = A,T,C or G

<400> 72  
 tattacggaa aaacacacca cataattcaa ctancaaaga anactgcttc agggcgtgta 60  
 aaatgaaag cttccaggca gttatctgat taaagaacac taaaagagg acaaggctaa 120  
 aagccgcagg atgtctacac tatancaggc gctatttggg ttggctggag gagctgtgga 180  
 aaacatggan agattgggtgc tgganacgc cgtggctatt cctcattgtt attacanagt 240  
 gaggttctct gtgtgcccac tggtttgaaa accgttctnc aataatgata gaatagtaca 300  
 cacatgagaa ctgaaatggc ccaaaccag aaagaaagcc caactagatc ctcagaanac 360  
 gcttctaggg acaataaccg atgaagaaaa gatggcctcc ttgtgcccc gtctgttatg 420  
 atttctctcc attgcagcna naaaccggtt ctcttaagca aacncaggty atgatggcna 480  
 aaatacacc cctcttgag naccnggagg a 511

<210> 73  
 <211> 499  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(499)  
 <223> n = A,T,C or G

<400> 73  
 cagtgccagc actggtgcc gtaccagtac caataacagt gccagtgcc gtgccagcac 60  
 cagtgggtggc ttcagtgtcg gtgccagcct gaccgccact ctcacatttg ggctcttcgc 120  
 tggccttggg ggagctgggt ccagcaccag tggcagctct ggtgcctgtg gtttctccta 180  
 caagtgagat tttagatatt gttaatcctg ccagctcttc tcttcaagcc aggggtgcac 240  
 ctgagaaacc tactcaacac agcactctag gcagccacta tcaatcaatt gaagttgaca 300  
 ctctgcatta aatctatttg ccatttctga aaaaaaaaa aaaaaaagg cgcccgctcg 360  
 antctagagg gcccgtttaa acccgctgat cagcctcgac tgtgccttct anttgccagc 420  
 catctgttgt ttgccctcc cccngtcct tccttgacct tggaaagtgc cactccact 480  
 gtcctttcct aantaaaat 499

<210> 74  
 <211> 537  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(537)  
 <223> n = A,T,C or G

<400> 74  
 tttcatagga gaacacactg aggagatact tgaagaattt ggattcagcc gogaagagat 60  
 ttatcagctt aactcagata aaatcattga aagtaataag gtaaaagcta gtctctaact 120  
 tccaggccca cggctcaagt gaatttgaat actgcattta cagtgtagag taacacataa 180  
 cattgtatgc atggaaacat ggaggaaacag tattacagtg toctaccact ctaatcaaga 240  
 aaagaattac agactctgat tctacagtga tgattgaatt ctaaaaatgg taatcattag 300  
 ggcttttgat ttataanact ttgggtactt atactaaatt atggtagtta tactgccttc 360  
 cagtttgctt gatataattg ttgatattaa gattcttgac ttatatattg aatgggttct 420  
 actgaaaaan gaatgatata ttcttgaaga catcgatata catttattta cactcttgat 480  
 tctacaatgt agaaaatgaa ggaaatgcc caaattgtat ggtgataaaa gtcccg 537

<210> 75  
 <211> 467  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(467)  
 <223> n = A,T,C or G

<400> 75  
 caaanacaat tgttcaaaag atgcaaatga tacactactg ctgcagctca caaacacctc 60  
 tgcataattac acgtacctcc tcctgctcct caagtagtgt ggtctatttt gccatcatca 120  
 cctgctgtct gcttagaaga acggcctttct gctgcaangg agagaaatca taacagacgg 180  
 tggcacaagg aggccatctt ttccatcatg gttattgtcc ctagaagcgt cttctgagga 240  
 tctagtgtgg ctttctttct ggggttgggc catttcantt ctcatgtgtg tactattcta 300  
 tcattattgt ataacggttt tcaaaccngt gggcacncag agaacctcac tctgtaataa 360  
 caatgaggaa tagccacggg gatctccagc accaaatctc tccatgttnt tccagagctc 420  
 ctccagccaa cccaaatagc cgctgctatn gtgtagaaca tccctgn 467

<210> 76  
 <211> 400  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(400)  
 <223> n = A,T,C or G

<400> 76  
 aagctgacag cattcgggcc gagatgtctc gctccgtggc cttagctgtg ctgcgcgtac 60  
 tctctctttc tggcctggag gctatccagc gtactccaaa gattcaggtt tactcacgtc 120  
 atccagcaga gaattgaaaag tcaaatttcc tgaattgcta tgtgtctggg ttcatccat 180  
 ccgacattga agttgactta ctgaagaatg gagagagaat tgaaaaagtg gagcattcag 240  
 acttgtcttt cagcaaggac tgggtctttc atctcttgta ctacactgaa ttcaccccca 300  
 ctgaaaaaga tgagtatgcc tgccgtgtga accatgtgac tttgtcacag cccaagatng 360  
 ttnagtggga tcganacatg taagcagcan catgggaggt 400

<210> 77  
 <211> 248  
 <212> DNA  
 <213> Homo sapien

<400> 77  
 ctggagtgcc ttggtgtttc aagccccctgc aggaagcaga atgcaccttc tgaggcacct 60  
 ccagctgccc cggcggggga tgcgaggctc ggagcacctc tgcccggctg tgattgtctc 120  
 caggcactgt tcatctcagc ttttctgtcc ctttgctccc ggcaagcgtc tctgctgaaa 180  
 gttcatatct ggagcctgat gtcttaacga ataaaggctc catgctccac ccgaaaaaaa 240  
 aaaaaaaa 248

<210> 78  
 <211> 201  
 <212> DNA  
 <213> Homo sapien

<400> 78

```

actagtccag tgtggtggaa ttccattgtg ttgggcccaa cacaatggct acctttaaca    60
tcaccagac cccgccctgc ccggtcccca cgctgctgct aacgacagta tgatgcttac    120
tctgtactc ggaaactatt tttatgtaat taatgtatgc tttcttgttt ataaatgcct    180
gatttaaaaa aaaaaaaaaa a                                     201

```

```

<210> 79
<211> 552
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(552)
<223> n = A,T,C or G

```

```

<400> 79
tccttttgtt aggtttttga gacaacccta gacctaaact gtgtcacaga cttctgaatg    60
tttaggcagt gctagtaatt tcctcgtaat gattctgtta ttactttcct attctttatt    120
cctctttcct ctgaagatta atgaagttga aaattgaggt ggataaatac aaaaaggtag    180
tgtgatagta taagtatcta agtgcagatg aaagtgtgtt atatatatcc attcaaaatt    240
atgcaagtta gtaattactc agggtttaact aaattacttt aatatgctgt tgaacctact    300
ctgttccttg gctagaaaaa attataaaca ggactttgtt agtttgggaa gccaaattga    360
taatattcta tgttctaaaa gttgggctat acataaanta tnaagaaata tggaatttta    420
ttccaggaa tatgggggtc atttatgaat antaccggg anagaagttt tgantnaaac    480
cngttttgtt taatacgtta atatgtcctn aatnaacaag gcntgactta tttccaaaaa    540
aaaaaaaaaa aa                                             552

```

```

<210> 80
<211> 476
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(476)
<223> n = A,T,C or G

```

```

<400> 80
acagggattt gagatgctaa ggccccagag atcgtttgat ccaaccctct tattttcaga    60
ggggaaaaatg gggcctagaa gttacagagc atctagctgg tgcgctggca cccctggcct    120
cacacagact cccgagtagc tgggactaca ggcacacagt cactgaagca ggccctgttt    180
gcaattcacg ttgccacctc caacttaaac attcttcata tgtgatgtcc ttagtcaacta    240
aggttaaact ttcccaccca gaaaaggcaa cttagataaa atcttagagt actttcatac    300
tcttctaagt cctcttccag cctcactttg agtcctcctt gggggttgat aggaantntc    360
tcttggtttt ctcaataaaa tctctatcca tctcatgttt aatttggtac gcntaaaaat    420
gctgaaaaaa ttaaatgtt ctggtttcnc tttaaaaaaa aaaaaaaaaa aaaaaa      476

```

```

<210> 81
<211> 232
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(232)
<223> n = A,T,C or G

```

```

<400> 81

```

```

tttttttttg tatgccntcn ctgtgnggtt attgttgctg ccaccctgga ggagcccagt    60
ttctttctgta tctttctttt ctggggggtc ttcttggtc tgccctcca ttcccagcct    120
ctcatcccca tcttgcaact ttgctagggt tggaggcgt ttcttggtag cccctcagag    180
actcagtcag cggaataag tcttaggggt ggggggtgtg gcaagccggc ct            232

```

```

<210> 82
<211> 383
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(383)
<223> n = A,T,C or G

```

```

<400> 82
aggcgggagc agaagctaaa gccaaagccc aagaagagtg gcagtgccag cactggtgcc    60
agtaccagta ccaataacat gccagtcca gtgccagcac cagtgggtggc ttcagtgtg    120
gtgccagcct gaccgccact ctcacatttg ggctcttcgc tggccttggg ggagctgggt    180
ccagcaccag tggcagctct ggtgcctgtg gttctccta caagtggat tttagatatt    240
gttaatcctg ccagtccttc tcttcaagcc aggggtgcac ctcagaaacc tactcaaac    300
agcactctng gcagccacta tcaatcaatt gaagttgaca ctctgcatta aatctatttg    360
ccatttcaaa aaaaaaaaaa aaa            383

```

```

<210> 83
<211> 494
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(494)
<223> n = A,T,C or G

```

```

<400> 83
accgaattgg gaccgctggc ttataagcga tcatgtcctc cagtattacc tcaacgagca    60
gggagatcga gtctatacgc tgaagaaatt tgaccgatg ggacaacaga cctgtctcagc    120
ccatcctgct cggttctccc cagatgacaa atactctcga caccgaatca ccatcaagaa    180
acgcttcaag gtgctcatga ccagcaacc gcgcctgtc ctctgagggt ccttaaaactg    240
atgtcttttc tgccacctgt taccctcgg agactccgta accaaactct tcggactgtg    300
agccctgatg cctttttgcc agccatactc tttggentcc agtctctcgt ggcgattgat    360
tatgcttggt tgaggcaatc atggtggcat caccatnaa gggaacacat ttganttttt    420
tttncatat tttaaattac naccagaata nttcagaata aatgaattga aaaactctta    480
aaaaaaaaa aaaa            494

```

```

<210> 84
<211> 380
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(380)
<223> n = A,T,C or G

```

```

<400> 84
gttggtagcc tatggcgtgg ccacggangg gtcctgagg cacgggacag tgacttccca    60
agtatcctgc gcgcgtctt ctaccgtccc tacctgcaga tcttcgggca gattccccag    120

```

```

gaggacatgg acgtggccct catggagcac agcaactgct cgtcggagcc cggcttctgg 180
gcacaccctc ctggggccca ggcgggcacc tgcgtctccc agtatgccaa ctggctgggtg 240
gtgctgctcc tcgtcatctt cctgctcgtg gccaaacatcc tgctggtcac ttgctcattg 300
ccatgttcag ttacacattc ggcaaagtac agggcaacag cnatctctac tgggaaggcc 360
agcgttnccg cctcatccgg                                     380

```

```

<210> 85
<211> 481
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(481)
<223> n = A,T,C or G

```

```

<400> 85
gagttagctc ctccacaacc ttgatgaggt cgtctgcagt ggcctctcgc ttcataccgc 60
tnccatcgct atactgtagg ttgcccacca cctcctgcat cttggggcgg ctaatatcca 120
ggaaactctc aatcaagtca ccgtcnatna aacctgtggc tggttctgtc ttccgctcgg 180
tgtgaaagga tctccagaag gagtgctcga tcttccccac acttttgatg actttattga 240
gtcgattctg catgtccagc aggaggttgt accagctctc tgacagttag gtcaccagcc 300
ctatcatgcc nttgaacgtg ccgaagaaca ccgagccttg tgtggggggg gnagtctcac 360
ccagattctg cattaccaga nagccgtggc aaaaganatt gacaactcgc ccaggngaa 420
aaagaacacc tcctggaagt gctngccgct cctcgtccnt tggtggnngc gcntnccttt 480
t

```

```

<210> 86
<211> 472
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(472)
<223> n = A,T,C or G

```

```

<400> 86
aacatcttcc tgtataatgc tgtgtaatat cgatccgatn ttgtctgctg agaattcatt 60
acttggaata gcaacttnaa gcctggacac tggattataa attcacaata tgcaacactt 120
taaacagtgt gtcaatctgc tcccttactt tgtcatcacc agtctgggaa taagggtatg 180
ccctattcac acctgttaaa agggcgctaa gcatttttga ttcaacatct ttttttttga 240
cacaagtccg aaaaaagcaa aagtaaacag ttnttaattt gttagccaat tcactttctt 300
catgggacag agccatttga tttaaaaagc aaattgcata atattgagct ttgggagctg 360
atatntgagc ggaagantag cttttctact tcaccagaca caactccttt catattggga 420
tgttnacnaa agttatgtct cttacagatg ggatgctttt gtggcaattc tg 472

```

```

<210> 87
<211> 413
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(413)
<223> n = A,T,C or G

```

```

<400> 87

```



```

agaaccagt atctctnaaa acaacctctc atacctgtg gacctaat tgtgtgcgtg      60
tgtgtgtgcg cgcatattat atagacaggc acatcttttt tacttttgta aaagcttatg    120
cctcttttgt atctatatct gtgaaagttt taatgatctg ccataatgtc ttggggacct    180
ttgtcttctg tgtaaatggt actagagaaa acacctatnt tatgagtcaa tctagttngt    240
tttattcgac atgaaggaaa tttccagatn acaacactna caaactctcc cttgactagg    300
ggggacaaaag aaaagcanaa ctgaacatna gaaacaattn cctggtgaga aattncataa    360
acagaaattg ggtngtatat tgaaanannng catcattnaa acgttttttt ttt          418

```

&lt;210&gt; 88

&lt;211&gt; 448

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(448)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 88

```

cgcagcgggt cctctctatc tagctccagc ctctgcctg ccccaactcc cgcgtccgc      60
gtcctagccn accatggccg ggcccctgcg cgcccgcgtg ctctgctgg ccatcctggc    120
cgtggccctg gccgtgagcc ccgcggcccg ctccagtcct ggcaagccgc cgcgcctggt    180
gggaggccca tggaccccg cgtggaagaag aaggtgtgcg gcgtgactg gactttgccg    240
tcggcnanta caacaaaccc gcaacnactt ttaccnagcn cgcgtgcag gttgtgccgc    300
cccaancaaa ttgttactng gggtaantaa ttcttggaag ttgaacctgg gccaaacnng    360
tttaccagaa ccnagccaat tngaacaatt ncccctccat aacagcccct tttaaaaagg    420
gaancantcc tgntcttttc caaat      448

```

&lt;210&gt; 89

&lt;211&gt; 463

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(463)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 89

```

gaattttgtg cactggccac tgtgatggaa ccattgggcc aggatgcttt gagtttatca      60
gtagtgtatc tgccaaagt ggtgtgtgaa catgagtatg taaaatgtca aaaaattagc    120
agaggtctag gtctgcatac cagcagacag tttgtccgtg tattttgtag ccttgaagtt    180
ctcagtgaca agttnnttct gatgcgaagt tctnattcca gtgttttagt cctttgcac    240
tttnatgttn agacttgcc ctntnaaatt gcttttgtnt tctgcaggta ctatctgtgg    300
tttaacaaaa tagaannact tctctgcttn gaanatttga atatcttaca tctnaaaatn    360
aattctctcc ccatannaaa acccangccc ttggganaat ttgaaaaang gntccttcnn    420
aattcnnana anttcagtn tcatacaaca naacngganc ccc          463

```

&lt;210&gt; 90

&lt;211&gt; 400

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(400)

&lt;223&gt; n = A,T,C or G

```

<400> 90
agggattgaa ggtctnttnt actgtcggac tgttcancca ccaactctac aagttgctgt      60
cttccactca ctgtctgtaa gcntnttaac ccagactgta tcttcataaa tagaacaaat      120
tcttcaccag tcacatcttc taggaacctt ttggattcag ttagtataag ctcttccact      180
tcctttgtta agacttcacg tggtaaagtc ttaagttttg tagaaaggaa ttttaattgct      240
cgttctctaa caatgtcctc tccttgaagt atttggtgta acaaccacc tnaagtccct      300
ttgtgcatcc attttaaata tacttaatag ggcattggtt cactagggtt aattctgcaa      360
gagtcactctg tctgcaaaaag ttgcgttagt atatctgcc      480

```

```

<210> 91
<211> 480
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(480)
<223> n = A,T,C or G

```

```

<400> 91
gagctcggat ccaataatct ttgtctgagg gcagcacaca tatncagtgc catggnaact      60
ggtctacccc acatggggagc agcatgccgt agntatataa ggtcattccc tgagtcagac      120
atgcctcttt gactaccgtg tgccagtgtt ggtgattctc acacacctcc nncogctctt      180
tgtggaaaaa ctggcacttg nctggaacta gcaagacatc acttacaaat tcaccacgga      240
gacacttgaa aggtgtaaca aagcgactct tgcatgtctt tttgtccctc cggcaccagt      300
tgcaataact aaccogctgg tttgcctcca tcacatttgt gatctgtagc tctggataca      360
tctcctgaca gtactgaaga acttcttctt ttgtttcaaa agcaactctt ggtgcctgtt      420
ngatcaggtt cccatttccc agtccgaatg ttcacatggc atatnttact tcccacaaaa      480

```

```

<210> 92
<211> 477
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(477)
<223> n = A,T,C or G

```

```

<400> 92
atacagccca natcccacca cgaagatgcy cttgttgact gagaacctga tgcggtcact      60
ggtcccgtg tagccccagc gactctccac ctgctggaag cgttgatgac tgactcctt      120
cccagcgagg cagcagcggg gccggtcaat gaactccact cgtggcttgg ggttgacggt      180
taantgcagg aagaggctga ccacctcgcg gtccaccagg atgcccgaat gtgcgggacc      240
tgcagcgaaa ctccctgatg gtcatgagcg ggaagcgaat gangcccagg gccttgccca      300
gaaccttccg cctgttctct ggcgtcacct gcagctgctg ccgctnacac tcggcctcgg      360
accagcgagc aaacggcggt gaacagccgc acctcacgga tgccantgt gtcgcgtcc      420
aggaacggcn ccagcgtgac caggtcaatg tcggtgaanc ctccgcggtt aatggcg      477

```

```

<210> 93
<211> 377
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(377)
<223> n = A,T,C or G

```

```

<400> 93
gaacggctgg accttgccctc gcattgtgct gctggcagga ataccttggc aagcagctcc      60
agtccgagca gcccagacc gctgccgccc gaagctaagc ctgcctctgg ccttcccctc      120
cgccccaatg cagaaccant agtgggagca ctgtgttttag agttaagagt gaacactgtn      180
tgattttact tgggaatttc ctctgttata tagcttttcc caatgctaata ttccaaacaa      240
caacaacaaa ataacatggt tgcctgttna gttgtataaa agtangtgat tctgtatnta      300
aagaaaatat tactgttaca tatactgctt gcaantttctg tattttattgg tncctctggaa      360
ataaatatat tattaata

```

<210> 94

<211> 495

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(495)

<223> n = A,T,C or G

```

<400> 94
ccctttgagg ggtaggggtc cagttcccag tggagaagaa aggccaggag aantgcgtgc      60
cgagctgang cagatttccc acagtgaccc cagagccctg ggctatagtc tctgaccctt      120
ccaaggaaag accaccttct ggggacatgg gctggagggc aggacctaga ggcaccaagg      180
gaaggcccca ttccgggggtc gttcccagag gaggaaggga aggggctctg tgtgcccccc      240
acgaggaana ggccctgant cctgggatca nacaccctt cactgtatc cccacacaaa      300
tgcaagctca ccaagggtccc ctctcagtcc ctccctaca ccctgaacgg nactggccc      360
acaccacccc agancancca cccgccatgg ggaatgttct caaggaatcg cngggcaacg      420
tggaactctng tcccnnaagg gggcagaatc tccaatagan gganngaacc cttgctnana      480
aaaaaaaaana aaaaaa

```

<210> 95

<211> 472

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(472)

<223> n = A,T,C or G

```

<400> 95
ggttacttgg ttctattgcc accacttagt ggatgtcatt tagaaccatt ttgtctgctc      60
cctctggaag ccttgccgag agcggacttt gtaattggtg gagaataact gctgaatttt      120
tagctgtttt gagttgattc gcaccactgc accacaactc aatatgaaaa ctatttnact      180
tatttattat cttgtgaaaa gtatacaatg aaaattttgt tcatactgta tttatcaagt      240
atgatgaaaa gcaatagata tatattcttt tattatgttn aattatgatt gccattatta      300
atcggcaaaa tgtggagtgt atgttctttt cacagtaata tatgcctttt gtaacttcac      360
ttggttattt tattgtaat gaattacaaa attcttaatt taagaaaatg gtangttata      420
tttanttcan taatttcttt ccttgtttac gttaattttg aaaagaatgc at              472

```

<210> 96

<211> 476

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

&lt;222&gt; (1)...(476)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 96

ctgaagcatt	tcttcaaact	tntctacttt	tgctattgat	acctgtagta	agttgacaat	60
gtggtgaaat	ttcaaaatta	tatgtaactt	ctactagttt	tactttctcc	cccaagtctt	120
ttttaactca	tgattttttac	acacacaatc	cagaacttat	tatatagcct	ctaagtcttt	180
attcttcaca	gtagatgatg	aaagagtcct	ccagtgtctt	gngcanaatg	ttctagntat	240
agctggatac	atacngtggg	agttctataa	actcatacct	cagtgggact	naaccaaaat	300
tgtgttagtc	tcaattccta	ccacactgag	ggagcctccc	aaatcactat	attcttatct	360
gcagggtactc	ctccagaaaa	acngacaggg	caggcttgca	tgaaaaagtn	acatctgcgt	420
tacaaagtct	atcttctctca	nangtctgtn	aaggaacaat	ttaatcttct	agcttt	476

&lt;210&gt; 97

&lt;211&gt; 479

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(479)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 97

actctttcta	atgctgatat	gatcttgagt	ataagaatgc	atatgtcact	agaatggata	60
aaataatgct	gcaaaactta	tgttcttatg	caaaatggaa	cgctaataga	acacagctta	120
caatcgcaaa	tcaaaactca	caagtgtcga	tctgtttag	atttagtgta	ataagactta	180
gattgtgctc	cttcggatat	gattgtttct	canatcttgg	gcaatnttcc	ttagtcaaat	240
caggctacta	gaattctggt	attggatatn	tgagagcatg	aaatttttaa	naatacactt	300
gtgattatna	aattaatcac	aaatttcact	tatacctgct	atcagcagct	agaaaaacat	360
ntnnttttta	natcaaagta	ttttgtgttt	ggaantgtnn	aaatgaaatc	tgaatgtggg	420
ttcnatctta	ttttttcccn	gacnactant	tnctttttta	gggnctattc	tganccatc	479

&lt;210&gt; 98

&lt;211&gt; 461

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 98

agtgacttgt	cctccaacaa	aacccttga	tcaagtttgt	ggcactgaca	atcagaccta	60
tgctagtcc	tgctacttat	tcgctactaa	atgcagactg	gaggggacca	aaaaggggca	120
tcaactccag	ctggattatt	ttggagcctg	caaactctatt	cctacttgta	cggactttga	180
agtgattcag	tttcctctac	ggatgagaga	ctggtcgaag	aatatcctca	tcagacttta	240
tgaagccact	ctgaacacgc	tggttatcta	gatgagaaca	gagaaataaa	gtcagaaaaat	300
ttacctggag	aaaagaggct	ttggctgggg	accatcccat	tgaaccttct	cttaaggact	360
ttaagaaaaa	ctaccacatg	ttgtgtatcc	tggtgcccgc	cgtttatgaa	ctgaccaccc	420
tttgaataaa	tcttgacgct	cctgaacttg	ctcctctgcg	a		461

&lt;210&gt; 99

&lt;211&gt; 171

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 99

gtggccgcgc	gcagggtgtt	cctcgtagcg	cagggccccc	tcccttcccc	aggcgtccct	60
cggcgccctc	gcggggccga	ggaggagcgg	ctggcggggtg	gggggagtg	gacccaccc	120
cggtgagaaa	agccttctct	agcgatctga	gaggcggtgc	ttgggggtac	c	171

<210> 100  
 <211> 269  
 <212> DNA  
 <213> Homo sapien

<400> 100  
 cgcccgcaag tgcaactcca gctggggccg tgcggacgaa gattctgccca gcagttggtc 60  
 cgactgcgac gacggcggcg gcgacagtcg caggtgcagc gcgggcgcct ggggtcttgc 120  
 aaggctgagc tgacgccgca gaggtcgtgt cacgtccac gaccttgacg ccgtcgggga 180  
 cagccggaac agagcccggt gaagcgggag gcctcgggga gcccctcggg aaggcgggcc 240  
 cgagagatac gcaggtgcag gtggccgcc 269

<210> 101  
 <211> 405  
 <212> DNA  
 <213> Homo sapien

<400> 101  
 tttttttttt ttttggaaac tactgcgagc acagcaggtc agcaacaagt ttatttttga 60  
 gctagcaagg taacagggtg gggcatgggt acatgttcag gtcaacttcc tttgtcgtgg 120  
 ttgattgggt tgtctttatg gggcggggt ggggtagggt aaacgaagca aataacatgg 180  
 agtgggtgca cctccctgt agaacctgtg tacaagctt ggggcagttc acctggtctg 240  
 tgaccgtcat tttcttgaca tcaatgttat tagaagtcag gatattcttt agagagtcca 300  
 ctgttcttga gggagattag ggtttcttgc caaatccaac aaaatccact gaaaaagtgt 360  
 gatgatcagt acgaataccg aggcattatc tcatatcggg ggcca 405

<210> 102  
 <211> 470  
 <212> DNA  
 <213> Homo sapien

<400> 102  
 tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 60  
 ggcacttaac ccatttttat ttcaaaatgt ctacaaattt aatcccatta tacggtattt 120  
 tcaaaatcta aattattcaa attagccaaa tccttaccaa ataataccca aaaatcaaaa 180  
 atatacttct ttacgcaaac ttgttacata aattaaataa atatatacgg ctggtgtttt 240  
 caaagtacaa ttatcttaac actgcaaca ttttaaggaa ctaaaataaa aaaaaacact 300  
 ccgcaaagggt taaagggaac acaaaattct tttacaacac cattataaaa atcatatctc 360  
 aaatcttagg ggaatatata cttcacacgg gatcttaact tttactcact ttgtttattt 420  
 ttttaacca ttgtttgggc ccaacacaat ggaatcccc ctggactagt 470

<210> 103  
 <211> 581  
 <212> DNA  
 <213> Homo sapien

<400> 103  
 tttttttttt ttttttttga cccctctt ataaaaaaca agttaccatt ttatttttact 60  
 tacacatatt tattttataa ttggtattag atattcaaaa ggcagctttt aaaatcaaac 120  
 taaatgaaa ctgccttaga tacataatc tttaggaatta gcttaaaatc tgctaaagt 180  
 gaaaatcttc tctagctctt ttgactgtaa atttttgact cttgtaaaac atccaaattc 240  
 atttttcttg tctttaaaat tatctaattc ttccattttt tccctattcc aagtcaattt 300  
 gcttctctag cctcatttcc tagctcttat ctactattag taagtggctt ttttcctaaa 360  
 agggaaaaca ggaagagaaa tggcacacaa acaaacatt ttatattcat atttctacct 420  
 acgttaataa aatagcattt tgtgaagcca gctcaaaaagg aggttagat ctttttatgt 480  
 ccatttttagt cactaaacga tatcaaatg ccagaatgca aaagggttgt gaacatttat 540  
 tcaaaagcta atataagata tttcacatac tcatctttct g 581

<210> 104  
<211> 578  
<212> DNA  
<213> Homo sapien

<400> 104  
tttttttttt tttttttttt tttttctctt cttttttttt gaaatgagga tgcagttttt 60  
cactctctag atagggcag aagaaaactc atctttccag ctttaaaata acaatcaaatt 120  
ctcttatgct atatacatatt ttaagttaaa ctaatgagtc actggcttat cttctcctga 180  
aggaaatctg ttcattcttc tcattcataat agttatatca agtactacct tgcataattga 240  
gaggtttttc ttctctattt acacatatat ttccatgtga atttgatca aacctttatt 300  
ttcatgcaaa ctagaaaata atgtttcttt tgcataagag aagagaacaa tatagcatta 360  
caaaactgct caaattgttt gttaagttat ccattataat tagttggcag gagctaatac 420  
aaatcacatt tacgacagca ataataaaac tgaagtacca gttaaatatc caaaaataatt 480  
aaaggaacat ttttagcctg ggtataatta gctaattcac tttacaagca tttattagaa 540  
tgaattcaca tgttattatt cctagcccaa cacaatgg 578

<210> 105  
<211> 538  
<212> DNA  
<213> Homo sapien

<400> 105  
tttttttttt tttttcagta ataatacagaa caataatttat ttttatattt aaaattcata 60  
gaaaagtgc ttacatttaa taaaagtttg tttctcaaag tgatcagagg aattagatat 120  
gtcttgaca ccaatattaa tttgaggaaa atacaccaa atacattaag taaattattt 180  
aagatcatag agcttgtaag tgaaaagata aaatttgacc tcagaaactc tgagcattaa 240  
aaatccacta tttagcaata aattactatg gacttcttgc ttttaattttg tgatgaatat 300  
gggtgtcac tggtaaacca acacattctg aaggatacat tacttagtga tagattctta 360  
tgtactttgc taatacgtgg atatgagttg acaagtttct ctttcttcaa tcttttaagg 420  
ggcgagaaat gaggaagaaa agaaaaggat tacgcatact gttctttcta tgggaaggatt 480  
agatatgttt cttttgcaa tattaataaa ataataatgt ttactactag tgaaaccc 538

<210> 106  
<211> 473  
<212> DNA  
<213> Homo sapien

<400> 106  
tttttttttt ttttttagtc aagtttctat ttttattata attaaagtct tggtcatttc 60  
atttattagc tctgcaactt acatatttaa attaaagaaa cgtttttagac aactgtacaa 120  
tttataaatg taagggtgcca ttattgagta atataattcct ccaagagtgg atgtgtccct 180  
tctccacca actaatgaac agcaacatta gtttaatttt attagtagat atacactgct 240  
gcaaacgcta attctcttct ccatcccat gtgatattgt gtatatgtgt gagttggtag 300  
aatgcatcac aatctacaat caacagcaag atgaagctag gctgggcttt cggtgaaaat 360  
agactgtgtc tgtctgaatc aaatgatctg acctatcctc ggtggcaaga actcttcgaa 420  
ccgcttctc aaaggcgctg ccacatttgt ggctctttgc acttgtttca aaa 473

<210> 107  
<211> 1621  
<212> DNA  
<213> Homo sapien

<400> 107  
cgccatggca ctgcagggca tctcgggtcat ggagctgtcc ggcctggccc egggcccggt 60  
ctgtgctatg gtccctggctg acttcggggc gcgtgtggta cgctgggacc ggcccggtc 120  
ccgctacgac gtgagccgct tgggccgggg caagcgctcg ctagtgtgg acctgaagca 180  
gccgcgggga gccgcgctg tgcggcgctc gtgcgaagcg tcggtgtgc tgcgtggagcc 240

```

cttcgccgc ggtgtcatgg agaaactcca gctgggcccc gagattctgc agcgggaaaa 300
tccaaggctt atttatgcca ggctgagtggt atttggccag tcaggaagct tctgccggtt 360
agctggccac gatatcaact atttggcttt gtcagggtgtt ctctcaaaaa ttggcagaag 420
tggtgagaat ccgtatgccc cgctgaatct cctggctgac tttgctggtg gtggccttat 480
gtgtgcactg ggcattataa tggctctttt tgaccgcaca cgcactgaca agggtcaggt 540
cattgatgca aatatggtgg aaggaacagc atatttaagt tcttttctgt ggaaaactca 600
gaaatcgagt ctgtgggaag cacctcgagg acagaacatg ttggatggtg gagcaccttt 660
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<210> 108  
 <211> 382  
 <212> PRT  
 <213> Homo sapien

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<400> 108
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20     25     30
Arg Val Asp Arg Pro Gly Ser Arg Tyr Asp Val Ser Arg Leu Gly Arg
35     40     45
Gly Lys Arg Ser Leu Val Leu Asp Leu Lys Gln Pro Arg Gly Ala Ala
50     55     60
Val Leu Arg Arg Leu Cys Lys Arg Ser Asp Val Leu Leu Glu Pro Phe
65     70     75     80
Arg Arg Gly Val Met Glu Lys Leu Gln Leu Gly Pro Glu Ile Leu Gln
85     90     95
Arg Glu Asn Pro Arg Leu Ile Tyr Ala Arg Leu Ser Gly Phe Gly Gln
100    105    110
Ser Gly Ser Phe Cys Arg Leu Ala Gly His Asp Ile Asn Tyr Leu Ala
115    120    125
Leu Ser Gly Val Leu Ser Lys Ile Gly Arg Ser Gly Glu Asn Pro Tyr
130    135    140
Ala Pro Leu Asn Leu Leu Ala Asp Phe Ala Gly Gly Gly Leu Met Cys
145    150    155    160
Ala Leu Gly Ile Ile Met Ala Leu Phe Asp Arg Thr Arg Thr Asp Lys
165    170    175
Gly Gln Val Ile Asp Ala Asn Met Val Glu Gly Thr Ala Tyr Leu Ser
180    185    190
Ser Phe Leu Trp Lys Thr Gln Lys Ser Ser Leu Trp Glu Ala Pro Arg
195    200    205
Gly Gln Asn Met Leu Asp Gly Gly Ala Pro Phe Tyr Thr Tyr Arg

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210	215	220
Thr Ala Asp Gly Glu Phe	Met Ala Val Gly Ala	Ile Glu Pro Gln Phe
225	230	235
Tyr Glu Leu Leu Ile Lys	Gly Leu Gly Leu Lys	Ser Asp Glu Leu Pro
245	250	255
Asn Gln Met Ser Met Asp	Asp Trp Pro Glu Met	Lys Lys Lys Phe Ala
260	265	270
Asp Val Phe Ala Lys Lys	Thr Lys Ala Glu Trp	Cys Gln Ile Phe Asp
275	280	285
Gly Thr Asp Ala Cys Val	Thr Pro Val Leu Thr	Phe Glu Glu Val Val
290	295	300
His His Asp His Asn Lys	Glu Arg Gly Ser Phe	Ile Thr Ser Glu Glu
305	310	315
Gln Asp Val Ser Pro Arg	Pro Ala Pro Leu Leu	Leu Asn Thr Pro Ala
325	330	335
Ile Pro Ser Phe Lys Arg	Asp Pro Phe Ile Gly	Glu His Thr Glu Glu
340	345	350
Ile Leu Glu Glu Phe Gly	Phe Ser Arg Glu Glu	Ile Tyr Gln Leu Asn
355	360	365
Ser Asp Lys Ile Ile Glu	Ser Asn Lys Val Lys	Ala Ser Leu
370	375	380

<210> 109  
 <211> 1524  
 <212> DNA  
 <213> Homo sapien

<400> 109	
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gagcgtctga agcgcacgtc ccagaagggt gacttggcac tgaaacagct gggacacatc	1020
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cagggaccac agaccctca ccactcacag attcctcaca ctggggaaat aaagccattt	1500
cagaggaaaa aaaaaaaaaa aaaa	1524

<210> 110  
 <211> 3410  
 <212> DNA



&lt;213&gt; Homo sapien

&lt;400&gt; 110

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<210> 111  
 <211> 1289  
 <212> DNA  
 <213> Homo sapien

<400> 111  
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 aagtgaatc agcagagcct ctgggtggat gtgtagaagg cacttcaaaa tgcataaacc 1260  
 tgttacaatg ttaaaaaaaa aaaaaaaaaa 1289

<210> 112  
 <211> 315  
 <212> PRT  
 <213> Homo sapien

<400> 112  
 Met Val Phe Thr Val Arg Leu Leu His Ile Phe Thr Val Asn Lys Gln  
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 20 25 30  
 Phe Phe Leu Phe Phe Leu Gly Val Trp Leu Val Ala Tyr Gly Val Ala  
 35 40 45  
 Thr Glu Gly Leu Leu Arg Pro Arg Asp Ser Asp Phe Pro Ser Ile Leu  
 50 55 60  
 Arg Arg Val Phe Tyr Arg Pro Tyr Leu Gln Ile Phe Gly Gln Ile Pro  
 65 70 75 80  
 Gln Glu Asp Met Asp Val Ala Leu Met Glu His Ser Asn Cys Ser Ser  
 85 90 95  
 Glu Pro Gly Phe Trp Ala His Pro Pro Gly Ala Gln Ala Gly Thr Cys  
 100 105 110  
 Val Ser Gln Tyr Ala Asn Trp Leu Val Val Leu Leu Val Ile Phe  
 115 120 125  
 Leu Leu Val Ala Asn Ile Leu Leu Val Asn Leu Leu Ile Ala Met Phe  
 130 135 140  
 Ser Tyr Thr Phe Gly Lys Val Gln Gly Asn Ser Asp Leu Tyr Trp Lys  
 145 150 155 160

Ala Gln Arg Tyr Arg Leu Ile Arg Glu Phe His Ser Arg Pro Ala Leu  
 165 170 175  
 Ala Pro Pro Phe Ile Val Ile Ser His Leu Arg Leu Leu Arg Gln  
 180 185 190  
 Leu Cys Arg Arg Pro Arg Ser Pro Gln Pro Ser Ser Pro Ala Leu Glu  
 195 200 205  
 His Phe Arg Val Tyr Leu Ser Lys Glu Ala Glu Arg Lys Leu Leu Thr  
 210 215 220  
 Trp Glu Ser Val His Lys Glu Asn Phe Leu Leu Ala Arg Ala Arg Asp  
 225 230 235 240  
 Lys Arg Glu Ser Asp Ser Glu Arg Leu Lys Arg Thr Ser Gln Lys Val  
 245 250 255  
 Asp Leu Ala Leu Lys Gln Leu Gly His Ile Arg Glu Tyr Glu Gln Arg  
 260 265 270  
 Leu Lys Val Leu Glu Arg Glu Val Gln Gln Cys Ser Arg Val Leu Gly  
 275 280 285  
 Trp Val Ala Glu Ala Leu Ser Arg Ser Ala Leu Leu Pro Pro Gly Gly  
 290 295 300  
 Pro Pro Pro Pro Asp Leu Pro Gly Ser Lys Asp  
 305 310 315

<210> 113  
 <211> 553  
 <212> PRT  
 <213> Homo sapien

<400> 113  
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 20 25 30  
 Ala Ala Gly Ile Thr Tyr Val Pro Pro Leu Leu Leu Glu Val Gly Val  
 35 40 45  
 Glu Glu Lys Phe Met Thr Met Val Leu Gly Ile Gly Pro Val Leu Gly  
 50 55 60  
 Leu Val Cys Val Pro Leu Leu Gly Ser Ala Ser Asp His Trp Arg Gly  
 65 70 75 80  
 Arg Tyr Gly Arg Arg Pro Phe Ile Trp Ala Leu Ser Leu Gly Ile  
 85 90 95  
 Leu Leu Ser Leu Phe Leu Ile Pro Arg Ala Gly Trp Leu Ala Gly Leu  
 100 105 110  
 Leu Cys Pro Asp Pro Arg Pro Leu Glu Leu Ala Leu Leu Ile Leu Gly  
 115 120 125  
 Val Gly Leu Leu Asp Phe Cys Gly Gln Val Cys Phe Thr Pro Leu Glu  
 130 135 140  
 Ala Leu Leu Ser Asp Leu Phe Arg Asp Pro Asp His Cys Arg Gln Ala  
 145 150 155 160  
 Tyr Ser Val Tyr Ala Phe Met Ile Ser Leu Gly Gly Cys Leu Gly Tyr  
 165 170 175  
 Leu Leu Pro Ala Ile Asp Trp Asp Thr Ser Ala Leu Ala Pro Tyr Leu  
 180 185 190  
 Gly Thr Gln Glu Glu Cys Leu Phe Gly Leu Leu Thr Leu Ile Phe Leu  
 195 200 205  
 Thr Cys Val Ala Ala Thr Leu Leu Val Ala Glu Glu Ala Ala Leu Gly  
 210 215 220  
 Pro Thr Glu Pro Ala Glu Gly Leu Ser Ala Pro Ser Leu Ser Pro His  
 225 230 235 240  
 Cys Cys Pro Cys Arg Ala Arg Leu Ala Phe Arg Asn Leu Gly Ala Leu

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Leu Pro Arg Leu His Gln Leu Cys Cys Arg Met Pro Arg Thr Leu Arg
      260      265      270
Arg Leu Phe Val Ala Glu Leu Cys Ser Trp Met Ala Leu Met Thr Phe
      275      280      285
Thr Leu Phe Tyr Thr Asp Phe Val Gly Glu Gly Leu Tyr Gln Gly Val
      290      295      300
Pro Arg Ala Glu Pro Gly Thr Glu Ala Arg Arg His Tyr Asp Glu Gly
305      310      315      320
Val Arg Met Gly Ser Leu Gly Leu Phe Leu Gln Cys Ala Ile Ser Leu
      325      330      335
Val Phe Ser Leu Val Met Asp Arg Leu Val Gln Arg Phe Gly Thr Arg
      340      345      350
Ala Val Tyr Leu Ala Ser Val Ala Ala Phe Pro Val Ala Ala Gly Ala
      355      360      365
Thr Cys Leu Ser His Ser Val Ala Val Val Thr Ala Ser Ala Ala Leu
      370      375      380
Thr Gly Phe Thr Phe Ser Ala Leu Gln Ile Leu Pro Tyr Thr Leu Ala
385      390      395      400
Ser Leu Tyr His Arg Glu Lys Gln Val Phe Leu Pro Lys Tyr Arg Gly
      405      410      415
Asp Thr Gly Gly Ala Ser Ser Glu Asp Ser Leu Met Thr Ser Phe Leu
      420      425      430
Pro Gly Pro Lys Pro Gly Ala Pro Phe Pro Asn Gly His Val Gly Ala
      435      440      445
Gly Gly Ser Gly Leu Leu Pro Pro Pro Pro Ala Leu Cys Gly Ala Ser
      450      455      460
Ala Cys Asp Val Ser Val Arg Val Val Val Gly Glu Pro Thr Glu Ala
465      470      475      480
Arg Val Val Pro Gly Arg Gly Ile Cys Leu Asp Leu Ala Ile Leu Asp
      485      490      495
Ser Ala Phe Leu Leu Ser Gln Val Ala Pro Ser Leu Phe Met Gly Ser
      500      505      510
Ile Val Gln Leu Ser Gln Ser Val Thr Ala Tyr Met Val Ser Ala Ala
      515      520      525
Gly Leu Gly Leu Val Ala Ile Tyr Phe Ala Thr Gln Val Val Phe Asp
      530      535      540
Lys Ser Asp Leu Ala Lys Tyr Ser Ala
545      550

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<210> 114
<211> 241
<212> PRT
<213> Homo sapien

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      <400> 114
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      20      25      30
Ser Ile Asp Gly Ala Ser Phe Leu Lys Ile Phe Gly Pro Leu Ser Ser
      35      40      45
Ser Ala Met Gln Phe Val Asn Val Gly Tyr Phe Leu Ile Ala Ala Gly
      50      55      60
Val Val Val Phe Ala Leu Gly Phe Leu Gly Cys Tyr Gly Ala Lys Thr
      65      70      75      80
Glu Ser Lys Cys Ala Leu Val Thr Phe Phe Ile Leu Leu Leu Ile
      85      90      95

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Phe Ile Ala Glu Val Ala Ala Ala Val Val Ala Leu Val Tyr Thr Thr  
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 Met Ala Glu His Phe Leu Thr Leu Leu Val Val Pro Ala Ile Lys Lys  
 115 120 125  
 Asp Tyr Gly Ser Gln Glu Asp Phe Thr Gln Val Trp Asn Thr Thr Met  
 130 135 140  
 Lys Gly Leu Lys Cys Cys Gly Phe Thr Asn Tyr Thr Asp Phe Glu Asp  
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 Ser Pro Tyr Phe Lys Glu Asn Ser Ala Phe Pro Pro Phe Cys Cys Asn  
 165 170 175  
 Asp Asn Val Thr Asn Thr Ala Asn Glu Thr Cys Thr Lys Gln Lys Ala  
 180 185 190  
 His Asp Gln Lys Val Glu Gly Cys Phe Asn Gln Leu Leu Tyr Asp Ile  
 195 200 205  
 Arg Thr Asn Ala Val Thr Val Gly Gly Val Ala Ala Gly Ile Gly Gly  
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 225 230 235 240  
 Gln

<210> 115  
 <211> 366  
 <212> DNA  
 <213> Homo sapien

<400> 115  
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 ttggttttgt aatccatctt gctttttccc cattggaact agtcattaac ccatctctga 180  
 actggttagaa aaacatctga agagctagtc tatcagcatc tgacaggtga attggatggt 240  
 tctcagaacc atttcaccca gacagcctgt ttctatcctg ttttaataaat tagtttgggt 300  
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 ttagtc 366

<210> 116  
 <211> 282  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(282)  
 <223> n = A,T,C or G  
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 gagaaatgag atnaaacaca atnttataaa gtctacttag agaagatcaa gtgacctcaa 120  
 agactttact attttcataat tttaagacac atgattttatc ctatttttagt aacctgggtc 180  
 atacgtttaa caaaggataa tgtgaacagc agagaggatt tgttggcaga aaatctatgt 240  
 tcaatctnga actatctana tcacagacat ttctattcct tt 282

<210> 117  
 <211> 305  
 <212> DNA  
 <213> Homo sapien

<220>

45

<221> misc\_feature  
 <222> (1)...(305)  
 <223> n = A,T,C or G

<400> 117  
 acacatgtcg cttcactgcc ttcttagatg cttctggtca acatanagga acagggacca 60  
 tatttatcct ccctcctgaa acaattgcaa aataanacaa aatatatgaa acaattgcaa 120  
 aataaggcaa aatatatgaa acaacaggtc tcgagatatt ggaaatcagt caatgaagga 180  
 tactgatccc tgatcactgt cctaattgcag gatgtgggaa acagatgagg tcacctctgt 240  
 gactgcccga gcttactgcc thtagagagt ttctangctg cagttcagac agggagaaat 300  
 tgggt 305

<210> 118  
 <211> 71  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(71)  
 <223> n = A,T,C or G

<400> 118  
 accaagtggt ntgaatctct gacgtgggga tctctgattc ccgcacaatc tgagtggaaa 60  
 aantcctggg t 71

<210> 119  
 <211> 212  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(212)  
 <223> n = A,T,C or G

<400> 119  
 actccggttg gtgtcagcag cacgtggcat tgaacatngc aatgtggagc ccaaaccaca 60  
 gaaaatgggg tgaaattggc caactttcta tnaacttatg ttggcaantt tgccaccaac 120  
 agtaagctgg cccttctaataaaaagaaaat tgaaagggtt ctcactaanc ggaattaant 180  
 aatggantca aganactccc aggcctcagc gt 212

<210> 120  
 <211> 90  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(90)  
 <223> n = A,T,C or G

<400> 120  
 actcgttgca natcaggggc cccccagagt caccgttgca ggagtccttc tgggtttgcc 60  
 ctccgccggc gcagaacatg ctgggggtgt 90

<210> 121  
 <211> 218

<212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(218)  
 <223> n = A,T,C or G

<400> 121

tgtancgtga anacgacaga nagggttgtc aaaaatggag aanccttgaa gtcattttga	60
gaataagatt tgctaaaaga tttggggcta aaacatgggtt attgggagac atttctgaag	120
atatncangt aaattangga atgaattcat gggtcttttg ggaattcctt tacgatngcc	180
agcatanact tcatgtgggg atancagcta cccttgta	218

<210> 122  
 <211> 171  
 <212> DNA  
 <213> Homo sapien

<400> 122

taggggtgta tgcaactgta aggacaaaaa ttgagactca actggcttaa ccaataaagg	60
catttgtag ctcatggaac aggaagtcgg atgggtgggc atcttcagtg ctgcatgagt	120
caccaccccg gcggggtcat ctgtgccaca ggtccctgtt gacagtgcgg t	171

<210> 123  
 <211> 76  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(76)  
 <223> n = A,T,C or G

<400> 123

tgtagcgtga agacnacaga atgggtgtgtg ctgtgctatc caggaacaca tttattatca	60
ttatcaanta ttgtgt	76

<210> 124  
 <211> 131  
 <212> DNA  
 <213> Homo sapien

<400> 124

acctttcccc aaggccaatg tcctgtgtgc taactggcgg gctgcaggac agctgcaatt	60
caatgtgctg ggtcatatgg aggggaggag actctaaaat agccaatttt attctcttgg	120
ttaagatttg t	131

<210> 125  
 <211> 432  
 <212> DNA  
 <213> Homo sapien

<400> 125

actttatcta ctggctatga aatagatggg ggaaaattgc gttaccaact ataccactgg	60
cttgaaaaag agtgatagc tcttcagagg acttgtgact tttgctcaga tgctgaagaa	120
ctacagtctg catttggcag aaatgaagat gaatttggat taaatgagga tgctgaagat	180
ttgcctcacc aaacaaaagt gaaacaactg agagaaaatt ttcaggaaaa aagacagtgg	240

47

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ctcttgaagt atcagtcact tttgagaatg tttcttagtt actgcatact tcatggatcc 300
catggtgggg gtcttgcatc tgtaagaatg gaattgattt tgcttttgca agaattctcag 360
caggaaacat cagaaccact attttctagc cctctgtcag agcaaaccctc agtgcctctc 420
ctctttgctt gt 432

```

```

<210> 126
<211> 112
<212> DNA
<213> Homo sapien

```

```

<400> 126
acacaacttg aatagtaaaa tagaaactga gctgaaattt ctaattcact ttctaaccat 60
agtaagaatg atatttcccc ccagggatca ccaaatattt ataaaaattt gt 112

```

```

<210> 127
<211> 54
<212> DNA
<213> Homo sapien

```

```

<400> 127
accacgaaac cacaaacaag atggaagcat caatccactt gccaaagcaca gcag 54

```

```

<210> 128
<211> 323
<212> DNA
<213> Homo sapien

```

```

<400> 128
acctcattag taattgtttt gttgtttcat ttttttctaa tgtctcccct ctaccagctc 60
acctgagata acagaatgaa aatggaagga cagccagatt tctcctttgc tctctgctca 120
ttctctctga agtctaggtt acccattttg gggaccattt ataggcaata aacacagttc 180
ccaaagcatt tggacagttt cttgttgtgt tttagaatgg ttttcctttt tcttagcctt 240
ttcctgcaaa aggtcactc agtcccttgc ttgctcagtg gactgggctc cccagggcct 300
aggtgcctt cttttccatg tcc 323

```

```

<210> 129
<211> 192
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(192)
<223> n = A,T,C or G

```

```

<400> 129
acatacatgt gtgtatattt ttaaatatca cttttgtatc actctgactt tttagcatatc 60
tgaaaacaca ctaacataat ttntgtgaac catgatcaga tacaacccaa atcattcatc 120
tagcacattc atctgtgata naaagatagg tgagtttcat ttccttcacy ttggccaatg 180
gataaacaaa gt 192

```

```

<210> 130
<211> 362
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature

```



48

<222> (1)...(362)  
 <223> n = A,T,C or G

<400> 130  
 ccctttttta tggaaatgagt agactgtatg tttgaanatt tanccacaac ctctttgaca 60  
 tataatgacg caacaaaaag gtgctgttta gtccatggt tcagtttatg cccctgacaa 120  
 gtttccattg tgttttgccg atcttctggc taatcgtggt atcctccatg ttattagtaa 180  
 ttctgtattc cattttgtta acgcctggta gatgtaacct gctangaggc taactttata 240  
 cttattttaa agctcttatt ttgtggtcat taaaatggca atttatgtgc agcactttat 300  
 tgcagcagga agcacgtgtg ggttggttgt aaagctcttt gctaactcta aaaagtaatg 360  
 gg 362

<210> 131  
 <211> 332  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(332)  
 <223> n = A,T,C or G

<400> 131  
 ctttttgaaa gatcgtgtcc actcctgtgg acatcttgtt ttaatggagt ttcccatgca 60  
 gtangactgg tatggttgca gctgtccaga taaaacatt tgaagagctc caaaatgaga 120  
 gttotcccag gttcgccctg ctgctccaag tctcagcagc agcctctttt aggaggcatc 180  
 ttctgaacta gattaaggca gcttgtaa atctgatgtgat ttggtttatt atccaactaa 240  
 cttccatctg ttatcactgg agaaagccca gactccccan gacnggtacg gattgtgggc 300  
 atanaaggat tgggtgaagc tggcgttgtg gt 332

<210> 132  
 <211> 322  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(322)  
 <223> n = A,T,C or G

<400> 132  
 acttttgcca ttttgtatat ataaacaatc ttgggacatt ctctgaaaa ctaggtgtcc 60  
 agtggctaag agaactcgat ttcaagcaat tctgaaagga aaaccagcat gacacagaat 120  
 ctcaaattcc caaacagggg ctctgtggga aaaatgaggg aggacctttg tatctcgggt 180  
 tttagcaagt taaaatgaan atgacaggaa aggcttattt atcaacaaag agaagagttg 240  
 ggatgcttct aaaaaaaact ttggtagaga aaataggaat gctnaatcct agggaagcct 300  
 gtaacaatct acaattggtc ca 322

<210> 133  
 <211> 278  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(278)  
 <223> n = A,T,C or G

<400> 133  
 acaagccttc acaagtttaa ctaaattggg attaatcttt ctgtanttat ctgcataatt 60  
 cttgtttttc tttccatctg gtcctctggg tgacaatttg tggaaacaac totattgcta 120  
 ctatttaaaa aaaatcacaa atctttccct ttaagctatg ttnaattcaa actattcctg 180  
 ctattcctgt tttgtcaaag aaattatatt tttcaaaata tgtntatttg tttgatgggt 240  
 cccacgaaac actaataaaa accacagaga ccagcctg 278

<210> 134  
 <211> 121  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(121)  
 <223> n = A,T,C or G

<400> 134  
 gtttanaaaa cttgttttagc tccatagagg aaagaatggt aaactttgta ttttaaaaca 60  
 tgattctctg aggttaaact tggttttcaa atgttatttt tacttgatt ttgcttttgg 120  
 t 121

<210> 135  
 <211> 350  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(350)  
 <223> n = A,T,C or G

<400> 135  
 acttanaacc atgcctagca catcagaatc cctcaaagaa catcagtata atcctataacc 60  
 atancaagtg gtgactggtt aagcgtgcga caaaggtcag ctggcacatt acttgtgtgc 120  
 aaacttgata cttttgttct aagtaggaac tagtatacag tncctaggan tggtagtcca 180  
 ggggtgcccc caactcctgc agccgctcct ctgtgccagn ccctgnaagg aactttcgt 240  
 ccacctaact caagccctgg gccatgctac ctgcaatttg ctgaacaaac gtttgctgag 300  
 ttcccaagga tgcaaagcct ggtgctcaac tcctggggcg tcaactcagt 350

<210> 136  
 <211> 399  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(399)  
 <223> n = A,T,C or G

<400> 136  
 tgtaccgtga agacgacaga agttgcatgg cagggacagg gcagggccga ggccagggtt 60  
 gctgtgattg tatccgaata ntcctcgtga gaaaagataa tgagatgacg tgagcagcct 120  
 gcagacttgt gtctgccttc aanaagccag acaggaaggc cctgcctgcc ttggctctga 180  
 cctggcgccc agccagccag ccacagggtg gcttcttcct tttgtggtga caacnccaag 240  
 aaaactgcag agggccaggg tcagggtgtna gtgggtangt gaccataaaa caccagggtgc 300  
 tcccaggaac ccgggcaaag gccatccca cctacagcca gcatgccac tggcgtgatg 360  
 ggtgcagang gatgaagcag ccagntgttc tgctgtggt 399

50

<210> 137  
 <211> 165  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(165)  
 <223> n = A,T,C or G

<400> 137  
 actggtgtgg tnggggtga tgctggtggt anaagttgan gtgacttcan gatggtgtgt 60  
 ggaggaagtg tgtgaacgta gggatgtaga ngttttggcc gtgctaaatg agcttcggga 120  
 ttggctggtc ccaactggtg tcaactgtcat tgggtggggt cctgt 165

<210> 138  
 <211> 338  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(338)  
 <223> n = A,T,C or G

<400> 138  
 actcactgga atgccacatt cacaacagaa tcagaggtct gtgaaaacat taatggctcc 60  
 ttaacttctc cagtaagaat cagggacttg aaatggaaac gttaacagcc acatgcccaa 120  
 tgctgggcag tctcccatgc cttccacagt gaaagggctt gagaaaaatc acatccaatg 180  
 tcatgtgttt ccagccacac caaaaggtgc ttgggggtgga gggctggggg catananggt 240  
 cangcctcag gaagcctcaa gttccattca gctttgccac tgtacattcc ccatntttaa 300  
 aaaaactgat gccttttttt tttttttttg taaaattc 338

<210> 139  
 <211> 382  
 <212> DNA  
 <213> Homo sapien

<400> 139  
 gggaatcttg gtttttggca tctggtttgc ctatagccga ggccactttg acagaacaaa 60  
 gaaagggact tcgagtaaga aggtgattta cagccagcct agtgcccgaa gtgaaggaga 120  
 attcaaacag acctcgtcat tctggtgtg agcctggtcg gctcaccgcc tatcatctgc 180  
 atttgcttta ctcaggtgct accggactct ggccctgat gtctgtagtt tcacaggatg 240  
 ccttatttgt cttctacacc ccacagggcc ccctacttct tcggatgtgt ttttaataat 300  
 gtcagctatg tgcccatcc tccttcatgc cctccctccc tttcctacca ctgctgagtg 360  
 gcctggaact tgtttaaagt gt 382

<210> 140  
 <211> 200  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(200)  
 <223> n = A,T,C or G

<400> 140  
 accaaanctt cttctgttg tgtnngattt tactataggg gtttngcttn ttctaaanct 60  
 acttttcatt taacancttt tgtaagtgt caggctgcac ttgctccat anaattattg 120  
 ttttcacatt tcaacttgta tgggtttgtc tcttanagca ttggtgaaat cacatatttt 180  
 atattcagca taaaggagaa 200

<210> 141  
 <211> 335  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(335)  
 <223> n = A,T,C or G

<400> 141  
 actttatttt caaaacactc atatgttgca aaaaacacat agaaaaataa agtttggtgg 60  
 ggggtgtgac taaacttcaa gtcacagact tttatgtgac agattggagc agggtttggt 120  
 atgcatgtag agaaccctaa ctaatttatt aaacaggata gaaacaggct gtctgggtga 180  
 aatgggtctg agaaccatcc aattcacctg tcagatgctg atanactagc tcttcagatg 240  
 tttttctacc agttcagaga tnggttaatg actanttcca atgggggaaa agcaagatgg 300  
 attcaaaaac caagtaattt taaacaaaga cactt 335

<210> 142  
 <211> 459  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(459)  
 <223> n = A,T,C or G

<400> 142  
 accagggttaa tattgccaca tatatccttt ccaattgcgg gctaaacaga cgtgtattta 60  
 ggggtgttta aagacaaccc agcttaatat caagagaaat tgtgaccttt catggagtat 120  
 ctgatggaga aaacactgag ttttgacaaa tcttatttta ttcagatagc agtctgatca 180  
 cacatgtgcc aacaacactc aaataataaa tcaaataatna tcagatgtta aagattggct 240  
 ttcaaacatc atagccaatg atgccccgct tgcctataat ctctccgaca taaaaccaca 300  
 tcaaacctc agtggccacc aaaccattca gcacagcttc cttaactgtg agctgtttga 360  
 agctaccagt ctgagcacta ttgactatnt ttttcangct ctgaatagct ctagggatct 420  
 cagcangggg gggaggaacc agctcaacct tggcgtant 459

<210> 143  
 <211> 140  
 <212> DNA  
 <213> Homo sapien

<400> 143  
 acatttcctt ccaccaagtc aggactcctg gcttctgtgg gagttcttat cacctgaggg 60  
 aaatccaaac agtctctcct agaaaggaat agtgtcacca accccaccca tctccctgag 120  
 accatccgac ttccctgtgt 140

<210> 144  
 <211> 164  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(164)  
 <223> n = A,T,C or G

<400> 144  
 acttcagtaa caacatacaa taacaacatt aagtgtatat tgccatcttt gtcattttct 60  
 atctatacca ctctcccttc tgaaaacaan aatcactanc caatcactta tacaatttg 120  
 aggcaattaa tccatatttg ttttcaataa ggaaaaaag atgt 164

<210> 145  
 <211> 303  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(303)  
 <223> n = A,T,C or G

<400> 145  
 acgtagacca tccaactttg tatttgtaat ggcaaacatc cagnagcaat tcctaaacaa 60  
 actggagggt atttataccc aattatccca ttcattaaca tgccctcctc ctcagggtat 120  
 gcaggacagc tatcataagt cggcccaggc atccagatac taccatttgt ataaaacttca 180  
 gtaggggagt ccatccaagt gacaggtcta atcaaaggag gaaatggaac ataagcccag 240  
 tagtaaaatn ttgcttagct gaaacagcca caaaagactt accgccgtgg tgattaccat 300  
 caa 303

<210> 146  
 <211> 327  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(327)  
 <223> n = A,T,C or G

<400> 146  
 actgcagctc aattagaagt ggtctctgac tttcatcanc ttctccctgg gctccatgac 60  
 actggcctgg agtgactcat tgctctggtt ggttgagaga gtccttttgc caacaggcct 120  
 ccaagtcagg gctgggattt gtttcccttc cacattctag caacaatatg ctggccactt 180  
 cctgaacagg gaggggtgga ggagccagca tggaacaagc tgccactttc taaagtagcc 240  
 agacttgccc ctgggcctgt cacacctact gatgaccttc tgtgacctgca ggatggaatg 300  
 taggggtgag ctgtgtgact ctatggt 327

<210> 147  
 <211> 173  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(173)  
 <223> n = A,T,C or G

<400> 147

```

acattgtttt tttagataa agcattgana gagctctcct taacgtgaca caatggaag 60
actggaacac ataccacat cttgttctg agggataatt ttctgataaa gtcttgctgt 120
atattcaagc acatatgtta tatattattc agttccatgt ttatagccta gtt 173

```

```

<210> 148
<211> 477
<212> DNA
<213> Homo sapien

```

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<220>
<221> misc_feature
<222> (1)...(477)
<223> n = A,T,C or G

```

```

<400> 148
acaaccactt tatctcatcg aatttttaac ccaaactcac tcaactgtgcc tttctatcct 60
atgggatata ttatttgatg ctccatttca tcacacatat atgaataata cactcatact 120
gccctactac ctgctgcaat aatcacattc ccttcctgtc ctgaccctga agccattggg 180
gtggtcctag tggccatcag tccangcctg caccttgagc ccttgagctc cattgctcac 240
nccanccac ctcaccgacc ccatcctctt acacagctac ctcttgctc tctaacccca 300
tagattatnt ccaaattcag tcaattaaat tactattaac actctaccg acatgtccag 360
caccactggt aagccttctc cagccaacac acacacacac acacncacac acacacatat 420
ccaggcacag gctacctcat cttcacaatc acccctttaa ttaccatgct atggtgg 477

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<210> 149
<211> 207
<212> DNA
<213> Homo sapien

```

```

<400> 149
acagttgtat tataatatca agaaataaac ttgcaatgag agcatttaag agggaagaac 60
taacgtatnt tagagagcca aggaagggtt ctgtggggag tgggatgtaa ggtggggcct 120
gatgataaat aagagtcagc caggtaagtg ggtggtgtg tatgggcaca gtgaagaaca 180
tttcaggcag agggaacagc agtgaaa 207

```

```

<210> 150
<211> 111
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(111)
<223> n = A,T,C or G

```

```

<400> 150
accttgattt cattgctgct ctgatggaaa cccaactatc taatttagct aaaacatggg 60
cacttaaatg tggtcagtgt ttggacttgt taactantgg catctttggg t 111

```

```

<210> 151
<211> 196
<212> DNA
<213> Homo sapien

```

```

<400> 151
agcgcggcag gtcattattga acattccaga tacctatcat tactcgatgc tgttgataac 60
agcaagatgg ctttgaactc aggtcacca ccagctattg gaccttacta tgaaaaccat 120
ggataccaac cggaaaaccc ctatcccga cagcccactg tggccccac tgtctacgag 180

```

gtgcatccgg ctcagt 196

<210> 152  
 <211> 132  
 <212> DNA  
 <213> Homo sapien

<400> 152  
 acagcacttt cacatgtaag aaggagagaaa ttcctaaatg taggagaaaag ataacagAAC 60  
 cttcccccttt tcatctagtgt gtggaaacct gatgctttat gttgacagga atagaaccag 120  
 gagggagttt gt 132

<210> 153  
 <211> 285  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(285)  
 <223> n = A,T,C or G

<400> 153  
 acaanaccca nganaggcca ctggccgtgg tgcattggcc tccaaacatg aaagtgtcag 60  
 cttctgtctt tatgtcctca tctgacaact ctttaccatt tttatcctcg ctcagcagga 120  
 gcacatcaat aaagtccaaa gtcttgact tggccttggc ttggaggaag tcatcaaac 180  
 cctggctagt gaggggtgcgg cggcgtcctt ggatgacggc atctgtgaag tctgtcacca 240  
 gtctgcaggc cctgtggaag cggcgtccac acggagtnag gaatt 285

<210> 154  
 <211> 333  
 <212> DNA  
 <213> Homo sapien

<400> 154  
 accacagtc tgttggggcca gggcttcatg accctttctg tgaaaagcca tattatcacc 60  
 accccaaatt tttccttaaa tatctttaac tgaaggggtc agcctcttga ctgcaaagac 120  
 cctaagccgg ttacacagct aactcccact ggccttgatt tgtgaaattg ctgctgcctg 180  
 attggcacag gagtccaagg tgttcagctc ccctcctcgg tggaaacgaga ctctgatttg 240  
 agtttcacaa attctcgggc cactcgtca ttgctcctct gaaataaaat ccggagaatg 300  
 gtcaggcctg tctcatccat atggatcttc cgg 333

<210> 155  
 <211> 308  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(308)  
 <223> n = A,T,C or G

<400> 155  
 actggaaata ataaaaccca catcacagtgt ttgtgtcaaa gatcatcagg gcatggatgg 60  
 gaaagtgtt ttgggaactgt aaagtgccta acacatgatc gatgattttt gttataatat 120  
 ttgaatcacg gtgcatacaa actctcctgc ctgctcctcc tgggccccag cccagcccc 180  
 atcacagctc actgctctgt tcatccaggc ccagcatgta gtggtgatt cttcttggt 240  
 gcttttagcc tccanaagtt tctctgaagc caaccaaacc tctangtga aggcattgctg 300

```

gccctggt                                     308

    <210> 156
    <211> 295
    <212> DNA
    <213> Homo sapien

    <400> 156
    accttgctcg gtgcttgga catattagga actcaaaata tgagatgata acagtgccta      60
    ttattgatta ctgagagaac tgttagacat ttagttgaag attttctaca caggaactga      120
    gaataggaga ttatgtttgg ccctcatatt ctctcctatc ctcccttgcc cattctatgt      180
    ctaatatatt ctcaatcaaa taaggttagc ataatcagga aatcgaccaa ataccaatat      240
    aaaaccagat gtctatcctt aagattttca aatagaaaac aaattaacag actat          295

    <210> 157
    <211> 126
    <212> DNA
    <213> Homo sapien

    <400> 157
    acaagtttaa atagtgtgt cactgtgcat gtgctgaaat gtgaaatcca ccacatttct      60
    gaagagcaaa acaaattctg tcatgtaatc tctatcttgg gtcgtgggta tatctgtccc      120
    cttagt                                     126

    <210> 158
    <211> 442
    <212> DNA
    <213> Homo sapien

    <220>
    <221> misc_feature
    <222> (1)...(442)
    <223> n = A,T,C or G

    <400> 158
    acccactggt cttggaaaca cccatcctta atacgatgat ttttctgtcg tgtgaaaatg      60
    aanccagcag gctgccccta gtcagtccct ccttcagag aaaaagagat ttgagaaagt      120
    gcctgggtaa ttcaccatta atttcctccc ccaaactctc tgagtcttcc cttaatattt      180
    ctggtgggtc tgaccaaagc aggtcatggt ttgttgagca tttgggatcc cagtgaagta      240
    natgtttgta gccttgcata cttagccctt cccacgcaca aacggagtgg cagagtgggtg      300
    ccaaccctgt tttccagtc cactagaca gattcacagt gcggaattct ggaagctgga      360
    nacagacggg ctctttgcag agccgggact ctgagangga catgagggcc tctgcctctg      420
    tgttcattct ctgatgtcct gt                                     442

    <210> 159
    <211> 498
    <212> DNA
    <213> Homo sapien

    <220>
    <221> misc_feature
    <222> (1)...(498)
    <223> n = A,T,C or G

    <400> 159
    acttccaggt aacgttgttg tttccgttga gcctgaactg atgggtgacg ttgtaggttc      60
    tccaacaaga actgaggttg cagagcgggt agggaagagt gctgttccag ttgcacctgg      120
    gctgctgtgg actgttgttg attcctcact acggccaag gttgtggaac tggcanaaag      180

```



```

gtgtgttgtt gganttgagc tcgggagggt gtggtagggt gtgggctctt caacaggggc 240
tgctgtgggt cggggangtg aangtggtgt gtcacttgag cttggccagc tctggaaagt 300
antanattct tcctgaaggc cagcgcttgt ggagctggca ngggtcantg ttgtgtgtaa 360
cgaaccagtg ctgtgtggg tgggtgtana tcctccacaa agcctgaagt tatgtgtcn 420
tcaggtaana atgtggtttc agtgtccctg ggcngctgtg gaaggttgta nattgtcacc 480
aaggaataa gctgtggt 498

```

```

<210> 160
<211> 380
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(380)
<223> n = A,T,C or G

```

```

<400> 160
acctgcatcc agcttccctg ccaaactcac aaggagacat caacctctag acagggaaac 60
agcttcagga tacttccagg agacagagcc accagcagca aaacaaatat tcccatgcct 120
ggagcatggc atagaggaag ctganaaaatg tggggtctga ggaagccatt tgagtctggc 180
cactagacat ctcatcagcc acttgtgtga agagatgccc catgacccca gatgcctctc 240
ccacccttac ctccatctca cacacttgag ctttccactc tgtataattc taacatcctg 300
gagaaaaatg gcagtttgac cgaacctgtt cacaacggta gaggctgatt tctaacgaaa 360
cttgtagaat gaagcctgga 380

```

```

<210> 161
<211> 114
<212> DNA
<213> Homo sapien

```

```

<400> 161
actccacatc cctctgagc aggcgggtgt cgttcaaggt gtatttggcc ttgcctgtca 60
cactgtccac tggcccctta tcacttggt gcttaatccc tcgaaagagc atgt 114

```

```

<210> 162
<211> 177
<212> DNA
<213> Homo sapien

```

```

<400> 162
actttctgaa tcgaatcaaa tgatacttag tgtagtttta atatcctcat atatatcaaa 60
gttttactac tctgataatt ttgtaaacca ggtaaccaga acatccagtc atacagcttt 120
tggatata taacttgga ataaccagc ctggtgatac ataaaactac tcactgt 177

```

```

<210> 163
<211> 137
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(137)
<223> n = A,T,C or G

```

```

<400> 163
catttataca gacaggcgtg aagacattca cgacaaaaac gcgaaattct atcccgtgac 60
canagaaggc agctacggct actcctacat cctggcgtgg gtggccttcg cctgcacctt 120

```

catcagcggc atgatgt

137

&lt;210&gt; 164

&lt;211&gt; 469

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(469)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 164

cttatcacaa	tgaatgttct	cctgggcagc	gttgtgatct	ttgccacctt	cgtgacttta	60
tgcaatgcat	catgctat	catacctaat	gagggagttc	caggagattc	aaccaggaaa	120
tgcatggatc	tcaaaggaaa	caaacaacca	ataaactcgg	agtggcagac	tgacaactgt	180
gagacatgca	cttgctacga	aacagaaatt	tcatgttgca	cccttgtttc	tacacctgtg	240
ggttatgaca	aagacaactg	ccaaagaatc	ttcaagaagg	aggactgcaa	gtatatcgtg	300
gtggagaaga	aggacccaaa	aaagacctgt	tctgtcagtg	aatggataat	ctaattgtgt	360
tctagttagc	acagggtcc	caggccaggc	ctcattctcc	tctggcctct	aatagtcaat	420
gattgtgtag	ccatgcctat	cagtaaaaag	atntttgagc	aaacacttt		469

&lt;210&gt; 165

&lt;211&gt; 195

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(195)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 165

acagtttttt	atanatatcg	acattgccgg	cacttgtgtt	cagtttcata	aagctggtgg	60
atccgctgtc	atccactatt	ccttggctag	agtaaaaatt	attcttatag	cccatgtccc	120
tgaggccgc	ccgcccgtag	ttctcgttcc	agtcgtcttg	gcacacaggg	tgccaggact	180
tcctctgaga	tgagt					195

&lt;210&gt; 166

&lt;211&gt; 383

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(383)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 166

acatcttagt	agtgtggcac	atcagggggc	catcagggtc	acagtcactc	atagcctcgc	60
cgagggtcga	gtccacacca	ccggtgtagg	tgtgtcfaat	cttgggcttg	gogcccacct	120
ttggagaagg	gatatgctgc	acacacatgt	ccacaaagcc	tgtgaactcg	ccaaagaatt	180
tttgcagacc	agcctgagca	aggggcggat	gttcagcttc	agctcctcct	tcgtcagggtg	240
gatgcccaacc	tcgtctangy	tccgtgggaa	gctggtgtcc	acntcaccta	caacctgggc	300
gangatctta	taaagaggct	ccnagataaa	ctccacgaaa	cttctctggg	agctgctagt	360
nggggccttt	ttggtgaact	ttc				383

&lt;210&gt; 167

<211> 247  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(247)  
 <223> n = A,T,C or G

<400> 167  
 acagagccag accttgGCCA taaatgaanc agagattaag actaaacccc aagtcganat 60  
 tggagcagaa actggagcaa gaagtgggcc tggggctgaa gtagagacca aggccactgc 120  
 tatanccata cacagagcca actctcaggc caaggcnatg gttggggcag anccagagac 180  
 tcaatctgan tccaaagtgg tggctggaac actggtcatg acanaggcag tgactctgac 240  
 tgangtc 247

<210> 168  
 <211> 273  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(273)  
 <223> n = A,T,C or G

<400> 168  
 acttctaagt ttctagaag tggaaggatt gtantcatcc tgaaaatggg tttacttcaa 60  
 aatccctcan ccttggttctt cacnactgtc tatactgana gtgtcatgtt tccacaaagg 120  
 gctgacacct gagcctgnat tttcactcat ccctgagaag ccctttccag taggggtggc 180  
 aattcccaac ttccttgcca caagcttccc aggttttctc ccctggaaaa ctccagcttg 240  
 agtcccagat acactcatgg gctgccctgg gca 273

<210> 169  
 <211> 431  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(431)  
 <223> n = A,T,C or G

<400> 169  
 acagccttgg cttccccaaa ctccacagtc tcagtgcaga aagatcatct tccagcagtc 60  
 agctcagacc aggggtcaaag gatgtgacat caacagtttc tggtttcaga acaggttcta 120  
 ctactgtcaa atgacccccc atacttcctc aaaggctgtg gtaagttttg cacagggtgag 180  
 ggcagcagaa aggggggtant tactgatgga caccatcttc tctgtatact ccacactgac 240  
 cttgccatgg gcaaaggccc ctaccacaaa aacaatagga tcaactgctg gcaccagctc 300  
 acgcacatca ctgacaaccg ggatggaaaa agaantgcc aacttcatac atccaactgg 360  
 aaagtgatct gatactggat tcttaattac cttcaaaagc ttctgggggc catcagctgc 420  
 tcgaacactg a 431

<210> 170  
 <211> 266  
 <212> DNA  
 <213> Homo sapien

59

<220>  
 <221> misc\_feature  
 <222> (1)...(266)  
 <223> n = A,T,C or G

<400> 170  
 acctgtgggc tgggctgtta tgcctgtgcc ggctgtctgaa agggagttca gaggtggagc 60  
 tcaaggagct ctgcaggcat ttgtccaanc ctctccanag canagggagc aacctacact 120  
 ccccgctaga aagacaccag attggagtcc tgggaggggg agttgggggtg ggcatattgat 180  
 gtatacttgt cacctgaatg aangagccag agaggaanga gacgaanatg anattggcct 240  
 tcaaagctag gggctctggca ggtgga 266

<210> 171  
 <211> 1248  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(1248)  
 <223> n = A,T,C or G

<400> 171  
 ggcagccaaa tcataaacgg cgaggactgc agcccgact cgcagccctg gcaggcggca 60  
 ctggtcatgg aaaacgaatt gttctgctcg ggcgtcctgg tgcattccga gtgggtgctg 120  
 tcagccgcac actgtttcca gaagtgtgag cagagctcct acaccatcgg gctgggcctg 180  
 cacagtcttg aggcggacca agagccaggg agccagatgg tggaggccag cctctccgta 240  
 cggcaccag agtacaacag acccttgctc gctaaccgacc tcatgctcat caagtggac 300  
 gaatccgtgt ccgagtctga caccatccgg agcatcagca ttgcttcgca gtgccctacc 360  
 gcggggaact cttgcctcgt ttctggctgg ggtctgctgg cgaacggcag aatgcctacc 420  
 gtgctgcagt gcgtgaacgt gtcgggtggtg tctgaggagg tctgcagtaa gctctatgac 480  
 ccgctgtacc accccagcat gttctgcgcc ggcggagggc aagaccagaa ggactcctgc 540  
 aacggtgact ctggggggcc cctgatctgc aacgggtact tgcagggcct tgtgtctttc 600  
 ggaaaagccc cgtgtggcca agttggcgtg ccagggtgtc acaccaacct ctgcaaattc 660  
 actgagtggg tagagaaaac cgtccaggcc agttaactct ggggactggg aacctatgaa 720  
 attgaccccc aaatacatcc tgcggaagga attcaggaat atctgttccc agccctcct 780  
 ccctcaggcc caggagtcca ggccccagc ccctcctccc tcaaaccaag ggtacagatc 840  
 cccagccctc cctccctcag acccaggagt ccagaccccc cagccctccc tccctcagac 900  
 ccaggagtcc agccctcctc ccctcagacc caggagtcca gacccccag cccctcctcc 960  
 ctccagacca ggggtccagg cccccaaccc ctccctccctc agactcagag gtccaagccc 1020  
 ccaaccnctc attccccaga cccagaggtc cagggtccag cccctcntcc ctccagacca 1080  
 gcggtccaat gccacctaga ctntccctgt acacagtgcc cccttggtgc acgttgaccc 1140  
 aacctacca gttggttttt catttttngt ccctttcccc tagatccaga aataaagttt 1200  
 aagagaagng caaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1248

<210> 172  
 <211> 159  
 <212> PRT  
 <213> Homo sapien

<220>  
 <221> VARIANT  
 <222> (1)...(159)  
 <223> Xaa = Any Amino Acid

<400> 172  
 Met Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro  
 1 5 10 15

60

```

Leu Leu Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser
      20      25      30
Glu Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr
      35      40      45
Ala Gly Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly
      50      55      60
Arg Met Pro Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu
      65      70      75      80
Glu Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe
      85      90      95
Cys Ala Gly Gly Gln Xaa Gln Xaa Asp Ser Cys Asn Gly Asp Ser
      100      105      110
Gly Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe
      115      120      125
Gly Lys Ala Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn
      130      135      140
Leu Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
      145      150      155

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<210> 173
<211> 1265
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(1265)
<223> n = A,T,C or G

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```

<400> 173
ggcagcccgcc actgcgagcc ctggcaggcg gcactgggtca tggaaaacga attgttctgc      60
tcgggcgctcc tgggtgcatcc gcagtgggtg ctgtcagccg cacactgttt ccagaactcc      120
tacaccatcg gctgggacct gcacagtctt gaggccgacc aagagccagg gagccagatg      180
gtggaggcca gcctctccgt acggcaccca gactacaaca gacccttgct cgctaacgac      240
ctcatgctca tcaagttgga cgaatccgtg tccgagtctg acaccatccg gagcatcagc      300
attgcttgcg agtgccttac cgcggggaac tcttgccctg tttctggctg gggctctgctg      360
gcgaacggtg agctcacggg tgtgtgtctg cctctttcaa ggaggtcctc tgcccagtcg      420
cgggggctga cccagagctc tgcgtcccag gcagaatgcc taccgtgctg cagtgcgtga      480
acgtgtcggg ggtgtctgag gaggtctgca gtaagctcta tgaccgctg taccacccca      540
gcatgttctg cgcggcgga gggcaagacc agaaggactc ctgcaacggt gactctgggg      600
ggcccctgat ctgcaacggg tacttgagg gccttgtgtc tttcgaaaaa gcccctgtg      660
gccaagtgg cgtgccagg gtctacacca acctctgcaa attcactgag tggatagaga      720
aaaccgtcca ggccagttaa ctctggggac tgggaaccca tgaaattgac ccccaaatac      780
atcctgcgga aggaattcag gaatatctgt tcccagcccc tcctccctca ggcccaggag      840
tccaggcccc cagcccctcc tcctcaaac caagggtaca gatccccagc cctcctccc      900
tcagacccag gaggccagac ccccagccc ctctccctc agaccagga gtccagcccc      960
tcctcctca gaccagagg tccagacccc ccagcccctc ctccctcaga cccaggggtt      1020
gaggcccca accctcctc cttcagagtc agaggtccaa gcccacaacc cctcgttccc      1080
cagacccaga ggttnnaggtc ccagcccctc ttccntcaga cccagnggtc caatgccacc      1140
tagattttcc ctgnacacag tgcccccttg tggnaangttg acccaacctt accagttggt      1200
ttttcatttt tngtccttt ccctagatc cagaataaaa gtttaagaga ngngcaaaaa      1260
aaaaa                                           1265

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```

<210> 174
<211> 1459
<212> DNA
<213> Homo sapien

```

<220>  
 <221> misc\_feature  
 <222> (1)...(1459)  
 <223> n = A,T,C or G

<400> 174  
 ggtcagccgc acactgtttc cagaagttag tgcagagctc ctacaccatc gggctgggccc 60  
 tgcacagtct tgaggccgac caagagccag ggagccagat ggtggaggcc agcctctccg 120  
 tacggcacc cagagtacaac agacccttgc tgcctaacga cctcatgctc atcaagttgg 180  
 acgaatccgt gtcagagtct gacaccatcc ggagcatcag cattgcttcg cagtgcccta 240  
 ccgcggggaa ctcttgccctc gtttctggct ggggtctgct ggcgaacggg gagctcacgg 300  
 gtgtgtgtct gccctcttca aggaggtcct ctgcccagtc gcgggggctg acccagagct 360  
 ctgctgccca ggcagaatgc ctaccgtgct gcagtgcgtg aacgtgtcgg tgggtgtctga 420  
 ngaggtctgc antaagctct atgaccgct gtaccacccc ancatgttct gcgccggcgg 480  
 agggcaagac cagaaggact cctgcaacgt gagagagggg aaaggggagg gcaggcgact 540  
 cagggaaggg tggagaaggg ggagacagag acacacaggg ccgcatggcg agatgcagag 600  
 atggagagac acacagggag acagtgacaa cttagagagag aaactgagag aaacagagaa 660  
 ataaacacag gaataaagag aagcaaagga agagagaaac agaaacagac atggggaggc 720  
 agaaacacac acacatagaa atgcagttga ccttccaaca gcatggggcc tgaggggcgt 780  
 gacctccacc caatagaaaa tctctttata acttttgact ccccaaaaac ctgactagaa 840  
 atagcctact gttgacgggg agccttacca ataacataaa tagtcgattt atgcatacgt 900  
 tttatgcatt catgatatac ctttgttga attttttgat atttctaagc tacacagttc 960  
 gtctgtgaat ttttttaaat tgttgcaact ctccataaat ttttctgatg tgtttattga 1020  
 aaaaatccaa gtataagtgg acttgtgcat tcaaaccagg gttgttcaag ggtcaactgt 1080  
 gtaccagag ggaacagtg acacagattc atagaggtga aacacgaaga gaaacaggaa 1140  
 aaatcaagac tctacaaaga ggtgggagc ggtggtcat gcctgtaac ccagcacttt 1200  
 gggaggcgag gcaggcagat cacttgaggg aaggagttca agaccagcct ggccaaaatg 1260  
 gtgaaatcct gtcgtacta aaaatacaaa agttagctgg atatgggtggc aggcgcctgt 1320  
 aatcccagct acttgggagg ctgaggcagg agaattgctt gaatatggga ggcagagggt 1380  
 gaagtgaagt gagatcacac cactatactc cagctggggc aacagagtaa gactctgtct 1440  
 caaaaaaaaa aaaaaaaaaa 1459

<210> 175  
 <211> 1167  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(1167)  
 <223> n = A,T,C or G

<400> 175  
 gcgcagccct ggcaggcggc actggtcatg gaaaacgaat tgttctgctc gggcgtcctg 60  
 gtgcatccgc agtgggtgct gtcagccgca cactgtttcc agaactccta caccatcggg 120  
 ctgggcctgc acagtcttga ggccgaccaa gagccaggga gccagatggt ggaggccagc 180  
 ctctccgtac ggcacccaga gtacaacaga ctcttgctcg ctaacgacct catgtctatc 240  
 aagttggacg aatccgtgtc cgagtctgac accatccgga gcatcagcat tgcttcgcag 300  
 tgcctaccg cgggggaactc ttgcctcgtn tctggctggg gtctgctggc gaacggcaga 360  
 atgcctaccg tgcgtcactg cgtgaacgtg tgggtgggtg ctgaggangt ctgcagtaag 420  
 ctctatgacc cgtgttacc cccagcatg ttctgcgcgg gcggagggca agaccagaag 480  
 gactcctgca acggtgactc tggggggccc ctgatctgca acgggtactt gcagggcctt 540  
 gtgtctttcg gaaaagcccc gtgtggccaa cttggcgtgc caggtgtcta caccacctc 600  
 tgcaaatca ctgagtggat agagaaaacc gtccagncca gtttaactctg gggactggga 660  
 acccatgaaa ttgaccccca aatacatcct gcggaangaa ttcaggaata tctgttccca 720  
 gcccctctc cctcaggccc aggagtccag gcccagcc cctcctcct caaaccaagg 780  
 gtacagatcc ccagcccctc ctccctcaga cccaggagtc cagaccccc agcccctcnt 840  
 cntcagacc caggagtcca gcccctctc cntcagacgc aggagtccag acccccagc 900

62

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contentccg tcagaccag ggggtgcagc ccccaacccc tcntcentca gagtcagagg 960
tccaagcccc caaccctcg ttccccagac ccagaggtnc aggtcccagc ccctcctccc 1020
tcagaccag cgggtccaatg ccacctagan tntccctgta cacagtgcgc ccttggggca 1080
ngttgaccca accttaccag ttggtttttc atttttgtc cctttcccct agatccagaa 1140
ataaagtnta agagaagcgc aaaaaaa 1167

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<210> 176  
 <211> 205  
 <212> PRT  
 <213> Homo sapien

<220>  
 <221> VARIANT  
 <222> (1)...(205)  
 <223> Xaa = Any Amino Acid

<400> 176

Met	Glu	Asn	Glu	Leu	Phe	Cys	Ser	Gly	Val	Leu	Val	His	Pro	Gln	Trp
1				5					10					15	
Val	Leu	Ser	Ala	Ala	His	Cys	Phe	Gln	Asn	Ser	Tyr	Thr	Ile	Gly	Leu
			20					25					30		
Gly	Leu	His	Ser	Leu	Glu	Ala	Asp	Gln	Glu	Pro	Gly	Ser	Gln	Met	Val
		35					40					45			
Glu	Ala	Ser	Leu	Ser	Val	Arg	His	Pro	Glu	Tyr	Asn	Arg	Leu	Leu	Leu
	50					55					60				
Ala	Asn	Asp	Leu	Met	Leu	Ile	Lys	Leu	Asp	Glu	Ser	Val	Ser	Glu	Ser
65					70				75					80	
Asp	Thr	Ile	Arg	Ser	Ile	Ser	Ile	Ala	Ser	Gln	Cys	Pro	Thr	Ala	Gly
			85						90					95	
Asn	Ser	Cys	Leu	Val	Ser	Gly	Trp	Gly	Leu	Leu	Ala	Asn	Gly	Arg	Met
		100						105					110		
Pro	Thr	Val	Leu	His	Cys	Val	Asn	Val	Ser	Val	Val	Ser	Glu	Xaa	Val
		115					120					125			
Cys	Ser	Lys	Leu	Tyr	Asp	Pro	Leu	Tyr	His	Pro	Ser	Met	Phe	Cys	Ala
		130					135				140				
Gly	Gly	Gly	Gln	Asp	Gln	Lys	Asp	Ser	Cys	Asn	Gly	Asp	Ser	Gly	Gly
145					150				155					160	
Pro	Leu	Ile	Cys	Asn	Gly	Tyr	Leu	Gln	Gly	Leu	Val	Ser	Phe	Gly	Lys
			165					170						175	
Ala	Pro	Cys	Gly	Gln	Leu	Gly	Val	Pro	Gly	Val	Tyr	Thr	Asn	Leu	Cys
		180					185						190		
Lys	Phe	Thr	Glu	Trp	Ile	Glu	Lys	Thr	Val	Gln	Xaa	Ser			
		195					200					205			

<210> 177  
 <211> 1119  
 <212> DNA  
 <213> Homo sapien

<400> 177

gcgcactcgc	agccctggca	ggcggcactg	gtcatggaaa	acgaattgtt	ctgctcgggc	60
gtcctggtgc	atccgcagtg	ggtgctgtca	gccgcacact	gtttccagaa	ctcctacacc	120
atcgggctgg	gcctgcacag	tcttgaggcc	gaccaagagc	cagggagcca	gatgggtggag	180
gccagcctct	ccgtacggca	cccagagtac	aacagaccct	tgctcgctaa	cgacctcatg	240
ctcatcaagt	tggacgaatc	cgtgtccgag	tctgacacca	tccggagcat	cagcattgct	300
tgcagtgccc	ctaccgcggg	gaactcttgc	ctcgtttctg	gctgggggtct	gctggcgaaac	360
gatgtgtgta	ttgccatcca	gtcccagact	gtgggaggct	gggagtgtga	gaagctttcc	420
caaccctggc	agggttgtag	catttcggca	acttccagtg	caaggacgtc	ctgctgcac	480

63

```

ctcactgggt gctcactact gctcactgca tcacccggaa cactgtgatc aactagccag 540
caccatagtt ctccgaagtc agactatcat gattactgtg ttgactgtgc tgtctattgt 600
actaaccatg ccgatgttta ggtgaaatta gcgtcacttg gcctcaacca tcttggtatc 660
cagttatcct cactgaattg agatttcctg cttcagtgtc agccattccc acataatttc 720
tgacctacag aggtgaggga tcatatagct cttcaaggat gctgggtactc ccctcacaaa 780
ttcatttctc ctgtttagt gaaagggtgcg ccctctggag cctcccaggg tgggtgtgca 840
ggtcacaatg atgaatgtat gatcgtgttc ccattacca aagcctttaa atccctcatg 900
ctcagtacac cagggcaggt ctagcatttc ttcatttagt gtatgctgtc cattcatgca 960
accacctcag gactcctgga ttctctgcct agttgagctc ctgcatgctg cctccttggg 1020
gaggtgaggg agagggccca tggttcaatg ggatctgtgc agttgtaaca cattaggtgc 1080
ttaataaaca gaagctgtga tgttaaaaaa aaaaaaaaaa 1119

```

<210> 178  
 <211> 164  
 <212> PRT  
 <213> Homo sapien

<220>  
 <221> VARIANT  
 <222> (1)...(164)  
 <223> Xaa = Any Amino Acid

```

<400> 178
Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp
 1          5          10          15
Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu
          20          25          30
Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val
          35          40          45
Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu Leu
          50          55          60
Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser
          65          70          75          80
Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly
          85          90          95
Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Asp Ala Val
          100          105          110
Ile Ala Ile Gln Ser Xaa Thr Val Gly Gly Trp Glu Cys Glu Lys Leu
          115          120          125
Ser Gln Pro Trp Gln Gly Cys Thr Ile Ser Ala Thr Ser Ser Ala Arg
          130          135          140
Thr Ser Cys Cys Ile Leu Thr Gly Cys Ser Leu Leu Leu Thr Ala Ser
          145          150          155          160
Pro Gly Thr Leu

```

<210> 179  
 <211> 250  
 <212> DNA  
 <213> Homo sapien

```

<400> 179
ctggagtgcc ttggtgtttc aagcccctgc aggaagcaga atgcaccttc tgaggcacct 60
ccagctgccc ccggccgggg gatgcgaggc tcggagcacc cttgcccggc tgtgattgct 120
gccaggcaat gttcatctca gcttttctgt ccctttgtct ccggcaagcg cttctgctga 180
aagttcatat ctggagcctg atgtcttaac gaataaaggt cccatgctcc acccgaaaaa 240
aaaaaaaaaa

```



64

<210> 180  
 <211> 202  
 <212> DNA  
 <213> Homo sapien

<400> 180  
 actagtccag tgtggtggaa ttccattgtg ttgggcccac cacaatggct acctttaaca 60  
 tcacccagac ccgcccctg ccggtgcccc acgctgctgc taacgacagt atgatgctta 120  
 ctctgctact cggaaactat ttttatgtaa ttaatgtatg ctttcttggt tataaatgcc 180  
 tgatttaaaa aaaaaaaaaa aa 202

<210> 181  
 <211> 558  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(558)  
 <223> n = A,T,C or G

<400> 181  
 tccytttkt naggtttkkg agacamccck agacctwaan ctgtgtcaca gacttcyngg 60  
 aatgtttagg cagtgcctag aatttcytcg taatgattct gttattactt tcctnattct 120  
 ttattcctct ttcttctgaa gattaatgaa gttgaaaatt gaggtggata aatacaaaaa 180  
 ggtagtgtga tagtataagt atctaagtgc agatgaaagt gtgttatata tatccattca 240  
 aaattatgca agtttagtaat tactcagggt taactaaatt actttaatat gctgttgaac 300  
 ctactctgtt ccttggctag aaaaaattat aaacaggact ttgttagttt gggaagccaa 360  
 attgataata ttctatgttc taaaagttgg gctatacata aattattaag aaatatggaw 420  
 ttttattccc aggaatatgg kgttcatttt atgaatatta cscrggatag awgtwtgagt 480  
 aaaaycagtt ttggtwaata ygtwaatatg tcmtaataaa acaakgcttt gacttatttc 540  
 caaaaaaaaa aaaaaaaa 558

<210> 182  
 <211> 479  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(479)  
 <223> n = A,T,C or G

<400> 182  
 acagggwttk grggatgcta agscccrga rwtggttga tccaaccctg gcttwttttc 60  
 agaggggaaa atggggccta gaagttacag mscatytagy tgggtgcgmg gcacccctgg 120  
 cstcacacag astcccgagt agctgggact acaggcacac agtcactgaa gcaggccctg 180  
 ttwgcaattc acgttgccac ctccaactta aacattcttc atatgtgatg tccttagtca 240  
 ctaaggttaa actttccac ccagaaaagg caacttagat aaaatcttag agtactttca 300  
 tactmttcta agtcctcttc cagcctcact kkgagtcctm cytgggggtt gataggaant 360  
 ntctcttggc tttctcaata aartctctat ycatctcatg ttttaatttg tacgcatara 420  
 awtgstgara aaattaaaat gttctggtty mactttaaaa aaaaaaaaaa aaaaaaaaaa 479

<210> 183  
 <211> 384  
 <212> DNA  
 <213> Homo sapien

65

&lt;400&gt; 183

aggcgggagc	agaagctaaa	gccaaagccc	aagaagagt	gcagtgccag	cactggtgcc	60
agtaccagta	ccaataacag	tgccagtgcc	agtgccagca	ccagtgggtg	cttcagtgtc	120
ggtgccagcc	tgaccgccac	tctcacattt	gggtctctcg	ctggccttgg	tggagctggt	180
gccagcacca	gtggcagctc	tggtgcctgt	ggtttctcct	acaagtgaga	ttttagatat	240
tgtaatacct	gccagtcttt	ctcttcaagc	cagggtgcat	cctcagaaac	ctactcaaca	300
cagcactcta	ggcagccact	atcaatcaat	tgaagttgac	actctgcatt	aratctattt	360
gccatttcaa	aaaaaaaaaa	aaaa				384

&lt;210&gt; 184

&lt;211&gt; 496

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(496)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 184

accgaattgg	gaccgctggc	ttataagcga	tcatgtyynt	ccrgtatkac	ctcaacgagc	60
agggagatcg	agtctatacg	ctgaagaaat	ttgacccgat	gggacaacag	acctgctcag	120
cccatcctgc	tccgtttctc	ccagatgaca	aatactctsg	acaccgaatc	accatcaaga	180
aacgcttcaa	ggtgctcatg	accagcaac	cgcgccctgt	cctctgaggg	tcccttaaac	240
tgatgtcttt	tctgccacct	gttacccttc	ggagactccg	taaccaaact	cttcggactg	300
tgagccctga	tgcccttttt	ccagccatac	tctttggcat	ccagtctctc	gtggcgattg	360
attatgcttg	tgtgaggcaa	tcatggtggc	atcacccata	aagggaacac	atttgacttt	420
tttttctcat	attttaaatt	actacmagaw	tattwmagaw	waaatgawtt	gaaaaactst	480
taaaaaaaaa	aaaaaa					496

&lt;210&gt; 185

&lt;211&gt; 384

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 185

gctggtagcc	tatggcgkgy	cccacggagg	ggctcctgag	gccacggrac	agtgacttcc	60
caagtatcyt	gcgcsgegtc	ttctaccgtc	cctacctgca	gatcttcggg	cagattcccc	120
aggaggacat	ggacgtggcc	ctcatggagc	acagcaactg	ytctcgggag	cccggcttct	180
gggcacaccc	tcctggggcc	caggcgggca	cctgcgtctc	ccagtatgcc	aactggctgg	240
tggtgctgct	cctcgtcctc	ttcctgctcg	tggccaacat	cctgctggtc	aacttgctca	300
ttgccatgtt	cagttacaca	ttcggcaaag	tacagggcaa	cagcgatctc	tactgggaag	360
gcgcagcgtt	accgcctcat	ccgg				384

&lt;210&gt; 186

&lt;211&gt; 577

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(577)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 186

gagttagctc	ctccacaacc	ttgatgaggt	cgtctgcagt	ggcctctcgc	ttcataccgc	60
tnccatcgctc	atactgtagg	tttgccacca	cytctctggca	tcttggggcg	gcntaatatt	120
ccaggaaaact	ctcaatcaag	tcaccgtcga	tgaacctgt	gggctgggtc	tgtcttcgcg	180

66

```

tcggtgtgaa aggatctccc agaaggagt ctcgatcttc cccacacttt tgatgacttt 240
attgagtgga ttctgcatgt ccagcaggag gttgtaccag ctctctgaca gtgagggtcac 300
cagccctatc atgccgttga mcgtgccgaa garcaccgag ccttgtgtgg gggkkgaaagt 360
ctcaccacaga ttctgcatta ccagagagcc gtggcaaaaag acattgacaa actcgcccgag 420
gtggaaaaaag amcamctcct ggargtgctn gccgctcctc gtcmgtttgtt ggcagcgctw 480
tccttttgac acacaaacaa gttaaaggca ttttcagccc ccagaaantt gtcacatcc 540
aagatntcgc acagcactna tccagttggg attaaat 577

```

&lt;210&gt; 187

&lt;211&gt; 534

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (534)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 187

```

aacatcttcc tgtataatgc tgtgtaatat cgatccgatn ttgtctgstg agaatycatw 60
actkggaaaa gmaacattaa agcctggaca ctggtattaa aattcacaat atgcaacact 120
ttaaacagtg tgtcaatctg ctcccyynac tttgtcatca ccagtctggg aakaagggtta 180
tgccctatcc acacctgtta aaagggcgct aagcattttt gattcaacat cttttttttt 240
gacacaagtc cgaaaaaaagc aaaagtaaac agttatyaat ttgttagcca attcactttc 300
ttcatgggac agagccatyt gatttaaaaa gcaaattgca taatattgag cttggggagc 360
tgatatttga gcggaagagt agcctttcta cttcaccaga cacaactccc tttcatattg 420
ggatgttnac naaagtwatg tctctwacag atgggatgct tttgtggcaa tttctgtctg 480
aggatctccc agtttattta ccacttgacac aagaaggcgt tttcttcctc aggc 534

```

&lt;210&gt; 188

&lt;211&gt; 761

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1) ... (761)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 188

```

agaaaccagt atctctnaaa acaacctctc ataccttggt gacctaatth tgtgtgcgtg 60
tgtgtgtgcg cgcataattat atagacaggc acatcttttt tactttttgta aaagcttatg 120
cctcttttgg atctatatct gtgaaagttt taatgatctg ccataatgct ttggggacct 180
ttgtcttctg tgtaaatggt actagagaaa acacctatnt tatgagtcaa tctagttngt 240
tttattcgac atgaaggaaa tttccagatn acaacactna caaactctcc ctkgackarg 300
ggggacaaaag aaaagcaaaa ctgamcataa raacaaatwa cctgggtgaga arttgcataa 360
acagaaatwr ggtagtatat tgaarnacag catcattaaa rmgttwtktt wttctccctt 420
gcaaaaaaca tgtacngact tcccggtgag taatgccaaag ttgttttttt tatnataaaa 480
cttgcccttc attacatggt tnaaagtggg gtgggtggcc aaaatattga aatgatggaa 540
ctgactgata aagctgtaca aataagcagt gtgcctaaca agcaacacag taatgttgac 600
atgcttaatt cacaaatgct aatttcatta taaatgtttg ctaaaataca ctttgaacta 660
ttttctgtn ttcccagagc tgagatntta gattttatgt agtatnaagt gaaaaantac 720
gaaaataata acattgaaga aaaaanaaaa aaaaaaaa a 761

```

&lt;210&gt; 189

&lt;211&gt; 482

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

67

<220>  
 <221> misc\_feature  
 <222> (1)...(482)  
 <223> n = A,T,C or G

<400> 189  
 tttttttttt tttgccgatn ctactatttt attgcaggan gtgggggtgt atgcaccgca 60  
 caccggggct atnagaagca agaaggaagg agggagggca cagccccttg ctgagcaaca 120  
 aagccgcctg ctgccttctc tgtctgtctc ctggtgcagg cacatgggga gaccttcccc 180  
 aaggcagggg ccaccagtcc aggggtggga atacaggggg tgggangtgt gcataagaag 240  
 tgataggcac aggccaccgc gtacagaccg ctcggtcctt gacaggtnga tttcgaccag 300  
 gtcattgtgc cctgcccagg cacagcgtn atctggaaaa gacagaatgc tttccttttc 360  
 aaatttggct ngtcatngaa ngggcanttt tccaanttng gctnggtctt ggtacncttg 420  
 gttcggccca gctccncgtc caaaaantat tcaccnctt ccnaattgct tgcnggnccc 480  
 cc 482

<210> 190  
 <211> 471  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(471)  
 <223> n = A,T,C or G

<400> 190  
 tttttttttt ttttaaaaca gtttttcaca aaaaaattta ttagaagaat agtggttttg 60  
 aaaactctcg catccagtga gaactacat acaccacatt acagctngga atgtntctcca 120  
 aatgtctggt caaatgatac aatggaacca ttcaatctta cacatgcacg aaagaacaag 180  
 cgcttttgac atacaatgca caaaaaaaaa aggggggggg gaccacatgg attaaaattt 240  
 taagtactca tcacatacat taagacacag ttctagtcca gtcnaaaatc agaactgcnt 300  
 tgaaaaaattt catgtatgca atccaacca agaacttnat tggatgatcat gantnctcta 360  
 ctacatnacc cttgatcatt gccaggaacn aaaagttnaa ancacncngt acaaaaaanaa 420  
 tctgtaattn anttcaacct cgtacngaa aaatnttntt tatacactcc c 471

<210> 191  
 <211> 402  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(402)  
 <223> n = A,T,C or G

<400> 191  
 gagggattga aggtctgttc tastgtcggm ctgttcagcc accaactcta acaagttgct 60  
 gtcttccact cactgtctgt aagcttttta acccagacwg tatcttcata aatagaacaa 120  
 attcttcacc agtcacatct tctaggacct ttttggtatc agttagtata agctcttcca 180  
 cttcctttgt taagacttca tctggtaaag tcttaagttt ttagaaagg aattyaattg 240  
 ctggttctct aacaatgtcc tctccttgaa gtatttggt gaacaacca cctaaagtcc 300  
 ctttgtgcat ccatttttaa tatacttaat agggcattgk tncactaggt taaattctgc 360  
 aagagtcacg tgtctgcaaa agttgcgtta gtatatctgc ca 402

<210> 192  
 <211> 601

<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(601)  
<223> n = A,T,C or G

<400> 192

gagctcggat	ccaataatct	ttgtctgagg	gcagcacaca	tatncagtgc	catggnaact	60
ggtctacccc	acatgggagc	agcatgccgt	agntatataa	ggtcattccc	tgagtcagac	120
atgcytyttt	gaytaccgtg	tgccaagtgc	tggtgattct	yaacacacyt	ccatcccgyt	180
cttttgtgga	aaaactggca	cttktctgga	actagcarga	catcacttac	aaattcaccc	240
acgagacact	tgaaggtgt	aacaaagcga	ytcttgcatt	gctttttgtc	cctccggcac	300
cagttgtcaa	tactaaccgc	ctggtttgcc	tccatcacat	ttgtgatctg	tagctctgga	360
tacatctcct	gacagtactg	aagaacttct	tcttttgttt	caaaagcarg	tcttggtgcc	420
tgttggatca	ggttcccatt	tcccagtcyg	aatgttcaca	tggcataatt	wacttcccac	480
aaaacattgc	gatttgaggc	tcagcaacag	caaatcctgt	tccggcattg	gctgcaagag	540
cctcgatgta	gccggccagc	gccaaaggcag	gcgccgtgag	ccccaccagc	agcagaagca	600
g						601

<210> 193  
<211> 608  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(608)  
<223> n = A,T,C or G

<400> 193

atacagccca	natcccacca	cgaagatgcg	cttgttgact	gagaacctga	tgcggtcact	60
ggtcccgtg	tagccccagc	gactctccac	ctgctggaag	cggttgatgc	tgactcytt	120
cccaacgcag	gcaymagcgg	gscgggtcaa	tgaactccay	tcgtggcttg	gggtkgacgg	180
tkaagtgcag	gaagaggctg	accacctcgc	ggtccaccag	gatgcccgac	tgtgcgggac	240
ctgcagcgaa	actcctcgat	ggtcatgagc	gggaagcgaa	tgaggcccag	ggccttgccc	300
agaaccttcc	gctgtttctc	tgcgctcacc	tgacgtgct	gccgctgaca	ctcgccctcg	360
gaccagcgga	caaacggcrt	tgaacagccg	cacctcacgg	atgccagtg	tgctcgctc	420
caggammgsc	accagcgtgt	ccaggtcaat	gtcgggtgaag	ccctccgagg	gtrattggcg	480
ctgcagtgtt	tttgtcgatg	ttctccaggc	acaggctggc	cagctgcggg	tcattcgaaga	540
gtcgcgcctg	cgtgagcagc	atgaaggcgt	tgtcggctcg	cagttcttct	tcaggaaactc	600
cagcaat						608

<210> 194  
<211> 392  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(392)  
<223> n = A,T,C or G

<400> 194

gaacggctgg	accttgccctc	gcattgtgct	tgctggcagg	gaataccttg	gcaagcagyt	60
ccagtcgcag	cagccccaga	ccgtgccgc	ccgaagctaa	gcctgcctct	ggccttcccc	120
tccgcctcaa	tgacgaacca	gtagtggag	cactgtgttt	agagttaaga	gtgaacactg	180

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tttgatttta cttgggaatt tcctctgtta tatagctttt cccaatgcta atttccaaac 240
aacaacaaca aaataacatg tttgcctgtt aagttgtata aaagtaggtg attctgtatt 300
taaagaaaat attactgtta catatactgc ttgcaatttc tgtatttatt gktnctstgg 360
aaataaatat agttattaaa ggtgtcant cc 392

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```

<210> 195
<211> 502
<212> DNA
<213> Homo sapien

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```

<220>
<221> misc_feature
<222> (1)...(502)
<223> n = A,T,C or G

```

```

<400> 195
ccsttkgagg ggtkaggkyc cagttyccga gtggaagaaa caggccagga gaagtgcgtg 60
ccgagctgag gcagatgttc ccacagtgc cccagagcc stgggstata gtytctgacc 120
cctcncaagg aaagaccacs ttctggggac atgggctgga gggcaggacc tagaggcacc 180
aagggaaggc ccatttccgg ggstgttccc cgaggaggaa gggaaggggc tctgtgtgcc 240
ccccasgagg aagaggccct gagtccctggg atcagacacc ccttcacgtg tatccccaca 300
caaatgcaag ctcaccaagg tcccctctca gtccccttcc stacaccctg amcggccact 360
gscscacacc caccagagc acgccaccg ccatggggar tgtgtcaag gartcgcnng 420
gcarcgtgga catctngtcc cagaaggggg cagaatctcc aatagangga ctgarcmstt 480
gctnanaaaa aaaaanaaaa aa 502

```

```

<210> 196
<211> 665
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(665)
<223> n = A,T,C or G

```

```

<400> 196
ggttacttgg tttcattgcc accacttagt ggatgtcatt tagaaccatt ttgtctgctc 60
cctctggaag ccttgcgcag agcggacttt gtaattgttg gagaataact gctgaatttt 120
wagctgtttk gagttgatts gcaccactgc acccacaact tcaatatgaa aacyawttga 180
actwatttat tatcttgtga aaagtataac aatgaaaatt ttgttcatac tgtattkatc 240
aagtatgatg aaaagcaawa gatatatatt cttttattat gttaaattat gattgccatt 300
attaatcggc aaaatgtgga gtgtatgttc ttttcacagt aatatatgcc ttttgtaact 360
tcacttggtt attttattgt aaatgartta caaaattctt aatttaagar aatggtatgt 420
watatttatt tcattaattt ctttctkgt ttacgtwaat tttgaaaaga wtgcatgatt 480
tcttgacaga aatcgatctt gatgctgttg aagtagtttg acccacatcc ctatgagttt 540
ttcttagaat gtataaagggt ttaggcccat cnaacttcaa agaaaaaat gaccacatac 600
tttgcaatca ggctgaaatg tggcatgctn ttctaattcc aactttataa actagcaaan 660
aagty 665

```

```

<210> 197
<211> 492
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(492)

```

<223> n = A,T,C or G

<400> 197

tttntttttt ttttttttgc aggaaggatt ccattttattg tggatgcatt ttcacaatat	60
atgtttattg gagcgatcca ttatcagtga aaagtatcaa gtgtttataa natttttagg	120
aaggcagatt cacagaacat gctngtcngc ttgcagtttt acctcgtana gatnacagag	180
aattatagtc naaccagtaa acnaggaatt tacttttcaa aagattaaat ccaaactgaa	240
caaaattcta ccttgaaact tactccatcc aaatatgtga ataanagtca gcagtgtac	300
attctcttct gaactttaga ttttctagaa aaatatgtaa tagtgatcag gaagagctct	360
tgttcaaaag tacaacnaag caatgttccc ttaccatagg ccttaattca aactttgatc	420
catttcactc ccatacggg agtcaatgct acctgggaca cttgtatttt gttcatnctg	480
ancntggctt aa	492

<210> 198

<211> 478

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(478)

<223> n = A,T,C or G

<400> 198

tttnttttgn atttcantct gtannaanta ttttcattat gtttattana aaaatatnaa	60
tgntntccacn acaaatcatn ttacntnagt aagaggccan ctacattgta caacatacac	120
tgagtatatt ttgaaaagga caagtttaaa gtanaacncat attgccganc atancacatt	180
tatacatggc ttgattgata tttagcacag canaaactga gtgagttacc agaaaanaa	240
natatatgtc aatcngattt aagatacaaa acagatccta tggtagatan catcntgtag	300
gagttgtggc tttatgttta ctgaaagtca atgcagttcc tgtacaaaga gatggccgta	360
agcattctag tacctctact ccatgggttaa gaatcgtaca cttatgttta catatgtnc	420
gggtaagaat tgtgttaagt naanttatgg agagggtccan gagaaaaatt tgatncaa	478

<210> 199

<211> 482

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(482)

<223> n = A,T,C or G

<400> 199

agtgacttgt cctccaacaa aacccttga tcaagtttgt ggcactgaca atcagacct	60
tgctagttcc tgcctctat tcgctactaa atgcagactg gaggggacca aaaaggggca	120
tcaactccag ctggattatt ttggagcctg caaatctatt cctacttgta cggactttga	180
agtgattcag tttcctctac ggatgagaga ctggctcaag aatatcctca tgcagcttta	240
tgaagccnac tctgaacacg ctggttatct nagatgagaa ncagagaaat aaagtcnaga	300
aaatttacct ggangaaaag aggttttngg ctggggacca tccattgaa ccttctctta	360
anggacttta agaanaaact accacatgtn tgtngtatcc tgggtgccngg ccgtttantg	420
aacntngacn ncacccttnt ggaatanant cttgacngcn tcctgaactt gctcctctgc	480
ga	482

<210> 200

<211> 270

<212> DNA

<213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(270)  
 <223> n = A,T,C or G

<400> 200  
 cgcccgcaag tgcaactcca gctggggccg tgcggacgaa gattctgcc a gcagttggtc 60  
 cgactgacgac gacggcgccg gcgacagtcg cagggtgcagc gcgggcgcct ggggtcttgc 120  
 aaggctgagc tgacgcccga gaggtcgtgt cacgtcccac gaccttgacg ccgtcgggga 180  
 cagccggaac agagcccgtt gaangcggga ggcctcgggg agcccctcgg gaaggcgccg 240  
 ccgagagata cgcagggtga ggtggccgcc 270

<210> 201  
 <211> 419  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(419)  
 <223> n = A,T,C or G

<400> 201  
 tttttttttt ttttggaaat tactgagcgc acagcaggtc agcaacaagt ttattttgca 60  
 gctagcaagg taacagggtta gggcatgggt acatgttcag gtcaacttcc tttgtcgtgg 120  
 ttgattgggt tgtctttatg ggggcggggg ggggtagggg aaancgaagc anaantaaca 180  
 tggagtgggt gcaccctccc tgtagaacct gggtacnaaa gcttggggca gttcacctgg 240  
 tctgtgaccg tcattttctt gacatcaatg ttattagaag tcaggatatac ttttagagag 300  
 tccactgtnt ctggaggagg attagggttt cttgccaana tccaancaaa atccacntga 360  
 aaaagtggga tgatncangt acngaatacc ganggcatan ttctcatant cgggtggcca 419

<210> 202  
 <211> 509  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(509)  
 <223> n = A,T,C or G

<400> 202  
 tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt 60  
 tggcacttaa tccattttta tttcaaaatg tctacaaant ttnaatncnc cattatacng 120  
 gtnattttnc aaaatctaaa nnttattcaa attnagcca aantccttac ncaaatnnaa 180  
 tacnncnaaa aatcaaaaat atacntntct ttcagcaaac ttngttacat aaattaaaaa 240  
 aatatatacg gctgggtgtt tcaaagtaca attatcttaa cactgcaaac atnttttnnaa 300  
 ggaactaaaa taaaaaaaaa cactnccgca aagggttaaag ggaacaacaa attcntttta 360  
 caacancnnc nattataaaa atcatatctc aaatcttagg ggaatatata cttcacacng 420  
 ggatcttaac ttttactnca ctttgtttat ttttttanaa ccattgtntt gggcccaaca 480  
 caatggnaat nccnccnccncc tggactagt 509

<210> 203  
 <211> 583  
 <212> DNA  
 <213> Homo sapien



<220>  
<221> misc\_feature  
<222> (1)...(583)  
<223> n = A,T,C or G

<400> 203  
tttttttttt ttttttttga ccccccctctt ataaaaaaca agttaccatt ttatttttact 60  
tacacatatt tatttttataa ttggtattag atattcaaaa ggcagctttt aaaatcaaac 120  
taaatggaaa ctgccttaga tacataattc ttaggaatta gcttaaaatc tgcctaaagt 180  
gaaaatcttc tctagctctt ttgactgtaa attttttgact cttgtaaaac atccaaattc 240  
atttttcttg tctttaaaaat tatctaactt ttccattttt tccctattcc aagtcaattt 300  
gcttctctag cctcatttcc tagctcttat ctactattag taagtggctt ttttcctaaa 360  
agggaaaaca ggaagagana atggcacaca aaacaacat tttatattca tatttctacc 420  
tacgttaata aaatagcatt ttgtgaagcc agctcaaaag aaggcttaga tccttttatg 480  
tccattttag tcaactaaacg atatcnaaag tgccagaatg caaaagggtt gtgaacattt 540  
attcaaaagc taatataaga tatttcacat actcatcttt ctg 583

<210> 204  
<211> 589  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(589)  
<223> n = A,T,C or G

<400> 204  
ttttttttnt tttttttttt ttttttntct tttttttttt ttganaatga ggatcgagtt 60  
tttcaactctc tagatagggc atgaagaaaa ctcatctttc cagctttaaa ataacaatca 120  
aatctcttat gctatatcat attttaagtt aaactaatga gtcactggct tatcttctcc 180  
tgaaggaaat ctgttcattc ttctcattca tatagttata tcaagtacta ccttgcatat 240  
tgagagggtt ttcttctcta ttacacata tatttccatg tgaatttgta tcaaaccctt 300  
attttcatgc aaactagaaa ataagtntt cttttgcata agagaagaga acaatatnag 360  
cattacaaaa ctgctcaaat tgtttggtta gnttatccat tataattagt tnggcaggag 420  
ctaatacaaa tcacatttac ngacnagcaa taataaaaact gaagtaccag ttaaatatcc 480  
aaaataatta aaggaacatt tttagcctgg gtataattag ctaattcact ttacaagcat 540  
ttattnagaa tgaattcaca tgttattatt cctnagccca acacaatgg 589

<210> 205  
<211> 545  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(545)  
<223> n = A,T,C or G

<400> 205  
ttttnttttt ttttttcagt aataatcaga acaatattta tttttatatt taaaattcat 60  
agaaaagtcg cttacattta ataaaagttt gtttctcaaa gtgatcagag gaattagata 120  
tngtcttgaa caccaatatt aatttgagga aaatacacca aaatacatta agtaaattat 180  
ttaagatcat agagcttgta agtgaaaaga taaaatttga cctcagaaac tctgagcatt 240  
aaaaatccac tattagcaaa taaattacta tggacttctt gctttaattt tgtgatgaat 300  
atgggggtgc actggtaaac caacacattc tgaaggatac attacttagt gatagattct 360  
tatgtacttt gctanatnac gtggatatga gttgacaagt ttctctttct tcaatctttt 420  
aaggggcnga ngaaatgagg aagaaaagaa aaggattacg catactgttc tttctatnng 480

aaggattaga tatgtttcct ttgccaatat taaaaaata ataatgttta ctactagtga 540  
aaccc 545

<210> 206  
<211> 487  
<212> DNA  
<213> Homo sapien  
  
<220>  
<221> misc\_feature  
<222> (1)...(487)  
<223> n = A,T,C or G

<400> 206  
tttttttttt ttttttagtc aagtttctna tttttattat aattaaagtc ttggtcattt 60  
cattttattag ctctgcaact tacatattta aattaaagaa acgttnttag acaactgtna 120  
caatttataa atgtaagggt ccattattga gtanatatat tcctccaaga gtggatgtgt 180  
cccttctccc accaactaat gaancagcaa cattagttaa attttattag tagatnatac 240  
actgctgcaa acgctaattc tcttctccat ccccatgtng atattgtgta tatgtgtgag 300  
ttggttagaa tgcatacanca atctnacaat caacagcaag atgaagctag gcntgggctt 360  
tcggtgaaaa tagactgtgt ctgtctgaat caaatgatct gacctatcct cgggtggcaag 420  
aactcttcga accgcttcct caaaggcngc tgccacattt gtggcntctn ttgcacttgt 480  
ttcaaaa 487

<210> 207  
<211> 332  
<212> DNA  
<213> Homo sapien  
  
<220>  
<221> misc\_feature  
<222> (1)...(332)  
<223> n = A,T,C or G

<400> 207  
tgaattggct aaaagactgc atttttanaa ctagcaactc ttatttcttt cctttaaaaa 60  
tacatagcat taaatcccaa atcctattta aagacctgac agcttgagaa ggtcactact 120  
gcatttatag gaccttctgg tggttctgct gttacntttg aantctgaca atccttgana 180  
atctttgcat gcagaggagg taaaagggtat tggattttca cagaggaana acacagcgca 240  
gaaatgaagg gccaggctt actgagcttg tccactggag ggctcatggg tgggacatgg 300  
aaaagaaggc agcctaggcc ctggggagcc ca 332

<210> 208  
<211> 524  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(524)  
<223> n = A,T,C or G

<400> 208  
agggcggtgt gcggaggggt ttactgtttt gtctcagtaa caataaatac aaaaagactg 60  
gttgtgttcc ggccccatcc aaccacgaag ttgatttctc ttgtgtgcag agtgactgat 120  
tttaaaggac atggagcttg tcacaatgtc acaatgtcac agtgtgaagg gcacactcac 180  
tcccgcgtga ttcacattta gcaaccaaca atagctcatg agtcatact tgtaaatact 240  
tttggcagaa tacttnttga aacttgcaaa tgataactaa gatccaagat atttcccaaa 300

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gtaaatagaa gtgggtcata atattaatta cctgttcaca tcagcttcca tttacaagtc 360
atgagcccag aactgacat caaactaagc ccacttagac tcctcaccac cagtctgtcc 420
tgtcatcaga caggaggctg tcaccttgac caaattctca ccagtcaatc atctatccaa 480
aaaccattac ctgatccact tccggtaatg caccaccttg gtga 524

```

```

<210> 209
<211> 159
<212> DNA
<213> Homo sapien

```

```

<400> 209
gggtgaggaa atccagagtt gccatggaga aaattccagt gtcagcattc ttgctccttg 60
tggccctctc ctacactctg gccagagata ccacagtcaa acctggagcc aaaaaggaca 120
caaaggactc tcgacccaaa ctgccccaga ccctctcca 159

```

```

<210> 210
<211> 256
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(256)
<223> n = A,T,C or G

```

```

<400> 210
actccctggc agacaaaggc agaggagaga gctctgtag ttctgtgttg ttgaactgcc 60
actgaatttc ttccacttg gactattaca tgccanttga gggactaatg gaaaaacgta 120
tggggagatt ttanccaatt tangtntgta aatggggaga ctggggcagg cgggagagat 180
ttgcagggtg naaatgggan ggctggtttg ttanatgaac agggacatag gaggtaggca 240
ccaggatgct aaatca 256

```

```

<210> 211
<211> 264
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(264)
<223> n = A,T,C or G

```

```

<400> 211
acattgtttt tttagataa agcattgaga gagctctcct taacgtgaca caatggaagg 60
actggaacac ataccacat cttgttctg agggataatt ttctgataaa gtcttgctgt 120
atattcaagc acatatgtta tatattatc agttccatgt ttatagccta gttaaggaga 180
ggggagatac attcngaaag aggactgaaa gaaatactca agtnggaaaa cagaaaaaga 240
aaaaaaggag caaatgagaa gcct 264

```

```

<210> 212
<211> 328
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(328)
<223> n = A,T,C or G

```

75

```

<400> 212
accacaaaat ccaatgctga atatttggct tcattattcc canattcttt gattgtcaaa      60
ggatttaatg ttgtctcagc ttgggcactt cagttaggac ctaaggatgc cagccggcag      120
gtttatatat gcagcaacaa tattcaagcg cgacaacagc ttattgaact tgcccgccag      180
ttnaatttca ttcccattga cttgggatcc ttatcatcag ccagagagat tgaaaattta      240
ccctacnac tctttactct ctgganaggc ccagtgggtg tagctataag cttggccaca      300
tttttttttc ctttattcct ttgtcaga                                     328

```

```

<210> 213
<211> 250
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(250)
<223> n = A,T,C or G

```

```

<400> 213
acttatgagc agagcgacat atccnagtgt agactgaata aaactgaatt ctctccagtt      60
taaagcattg ctactgaag ggatagaagt gactgccagg agggaaagta agccaaggct      120
cattatgcca aagganatat acatttcaat tctccaaact tcttcctcat tccaagagtt      180
ttcaatattt gcataacct gctgataanc catgttaana aacaaatata tctctnacct      240
tctcatcggt                                     250

```

```

<210> 214
<211> 444
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(444)
<223> n = A,T,C or G

```

```

<400> 214
acccagaatc caatgctgaa tatttggctt cattattccc agattctttg attgtcaaag      60
gatttaatgt tgtctcagct tgggcacttc agttaggacc taaggatgcc agccggcagg      120
tttatatatg cagcaacaat attcaagcgc gacaacaggt tattgaactt gcccgccagt      180
tgaatttcat tcccattgac ttgggatcct tatcatcagc canagagatt gaaaatttac      240
ccctacgact ctttactctc tggagagggc cagtgggtgt agctataagc ttggccacat      300
ttttttttcc tttattcctt tgtcagagat gcgattcatc catatgctan aaaccaacag      360
agtgactttt acaaaattcc tataganatt gtgaataaaa ccttacctat agttgccatt      420
actttgctct ccctaataata cctc                                     444

```

```

<210> 215
<211> 366
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(366)
<223> n = A,T,C or G

```

```

<400> 215
acttatgagc agagcgacat atccaagtgt anactgaata aaactgaatt ctctccagtt      60

```

taaagcattg	ctcactgaag	ggatagaagt	gactgccagg	agggaaagta	agccaaggct	120
cattatgcca	aagganatat	acattttcaat	tctccaaact	tcttcctcat	tccaagagtt	180
ttcaatattt	gcatgaacct	gctgataagc	catgttgaga	aacaaatata	tctctgacct	240
tctcatcggt	aagcagaggc	tgtaggcaac	atggaccata	gcgaanaaaa	aacttagtaa	300
tccaagctgt	tttctacact	gtaaccaggt	ttccaaccaa	ggtggaaatc	tcctatactt	360
ggtgcc						366

<210> 216  
 <211> 260  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(260)  
 <223> n = A,T,C or G

ctgtataaac	agaactccac	tgcanagagg	agggccgggc	caggagaatc	tccgcttgct	60
caagacaggg	gcctaaggag	ggtctccaca	ctgctnntaa	gggctnttnc	atTTTTTTat	120
taataaaaaag	tnnaaaaggc	ctcttctcaa	ctTTTTTccc	ttnggctgga	aaatttaaaa	180
atcaaaaatt	tcctnaagtt	ntcaagctat	catatatact	ntatcctgaa	aaagcaacat	240
aattcttctt	tccctccttt					260

<210> 217  
 <211> 262  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(262)  
 <223> n = A,T,C or G

acctacgtgg	gtaagtttan	aatgtttata	atttcaggaa	naggaacgca	tataattgta	60
tcttgccctat	aattttctat	tttaataagg	aaatagcaaa	ttgggggtgg	gggaatgtag	120
ggcattctac	agtttgagca	aatgcaatt	aatgtggaa	ggacagcact	gaaaaatttt	180
atgaataato	tgtatgatta	tatgtctcta	gagtagattt	ataattagcc	acttacccta	240
atataccttca	tgcttgtaaa	gt				262

<210> 218  
 <211> 205  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(205)  
 <223> n = A,T,C or G

accaaggtgg	tgcatcacg	gaantggatc	aangacacca	tcgtggccaa	cccctgagca	60
cccctatcaa	ctcccccttg	tagtaaaact	ggaaccttgg	aatgaccag	gccaagactc	120
aggcctcccc	agttctactg	acctttgtcc	ttangtntna	ngtccagggt	tgctaggaaa	180
anaaatcagc	agacacaggt	gtaaa				205

<210> 219

77

<211> 114  
 <212> DNA  
 <213> Homo sapien

<400> 219  
 tactgttttg tctcagtaac aataaatata aaaagactgg ttgtgttccg gcccacatcca 60  
 accacgaagt tgatttctct tgtgtgcaga gtgactgatt ttaaaggaca tgga 114

<210> 220  
 <211> 93  
 <212> DNA  
 <213> Homo sapien

<400> 220  
 actagccagc acaaaaggca gggtagcctg aattgctttg tgctctttac atttctttta 60  
 aaataagcat ttagtgctca gtcctactg agt 93

<210> 221  
 <211> 167  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(167)  
 <223> n = A,T,C or G

<400> 221  
 actangtgca ggtgcgcaca aatatttgtc gatattccct tcatcttgga ttccatgagg 60  
 tcttttgccc agcctgtggc tctactgtag taagtttctg ctgatgagga gccagnatgc 120  
 ccccactac ctccctgac gctcccana aatcacccaa cctctgt 167

<210> 222  
 <211> 351  
 <212> DNA  
 <213> Homo sapien

<400> 222  
 agggcggtgt gcgaggggcg gtactgacct cattagtagg aggatgcatt ctggcacccc 60  
 gttcttcacc tgtccccaa tccttaaaag gccatactgc ataaagtcaa caacagataa 120  
 atgtttgctg aattaaagga tggatgaaaa aaattaataa tgaatttttg cataatccaa 180  
 ttttctcttt tatatttcta gaagaagttt ctttgagcct attagatccc gggaatcttt 240  
 taggtgagca tgattagaga gcttgtaggt tgcttttaca tatatctggc atatttgagt 300  
 ctcgtatcaa aacaatagat tggtaaaggt ggtattattg tattgataag t 351

<210> 223  
 <211> 383  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(383)  
 <223> n = A,T,C or G

<400> 223  
 aaaacaaaca acaaaaaaaa acaattcttc attcagaaaa attatcttag ggactgatat 60  
 tggtaattat ggtcaattta atwrtttkt ggggcatttc cttacattgt cttgacaaga 120

ttaaaatgtc	tgtgccaaaa	ttttgtat	tatttgaga	cttcttatca	aaagtaatgc	180
tgccaaagga	agtctaagga	attagtagtg	ttcccmtcac	ttgtttggag	tgtgctattc	240
taaaagattt	tgatttcctg	gaatgacaat	tatattttaa	ctttggtggg	ggaaanagtt	300
ataggaccac	agtcttcact	tctgatactt	gtaaattaat	cttttatigc	acttgttttg	360
accattaagc	tatatgttta	aaa				383

<210> 224  
 <211> 320  
 <212> DNA  
 <213> Homo sapien

<400> 224						
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&lt;213&gt; Homo sapien

&lt;400&gt; 227

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&lt;210&gt; 228

&lt;211&gt; 744

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 228

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&lt;210&gt; 229

&lt;211&gt; 300

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 229

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&lt;210&gt; 230

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 230

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81

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&lt;210&gt; 240

&lt;211&gt; 300

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 240

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&lt;210&gt; 241

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 241

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&lt;210&gt; 242

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 242

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&lt;210&gt; 243

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 243

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&lt;210&gt; 244

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&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 244

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&lt;210&gt; 245

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 245

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&lt;210&gt; 246

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&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 246

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&lt;210&gt; 247

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&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 247

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a						301

&lt;210&gt; 248

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 248

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85

&lt;213&gt; Homo sapien

&lt;400&gt; 253

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gatttttttt	cttagagaac	cacaaaacat	aaaaggagca	agtcggactg	aatacctgtt	240
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g						301

&lt;210&gt; 254

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 254

cgctgcgcct	ttcccttggg	ggagggggcaa	ggccagaggg	ggtccaagtg	cagcacgagg	60
aacttgacca	attcccttga	agcgggtggg	ttaaaccctg	taaatgggaa	caaaatcccc	120
ccaaatctct	tcactttacc	ctggtggact	cctgactgta	gaattttttg	gttgaacaaa	180
gaaaaaata	aagctttgga	cttttcaagg	ttgcttaaca	ggtactgaaa	gactggcctc	240
acttaaaactg	agccaggaaa	agctgcagat	ttattaatgg	gtgtgttagt	gtgcagtgcc	300
t						301

&lt;210&gt; 255

&lt;211&gt; 302

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 255

agcttttttt	tttttttttt	tttttttttt	ttcattaaaa	aatagtgctc	tttattataa	60
attactgaaa	tgtttctttt	ctgaatataa	atataaatat	gtgcaaagtt	tgacttggat	120
tgggattttg	ttgagttctt	caagcatctc	ctaataccct	caagggcctg	agtagggggg	180
aggaaaaagg	actggaggty	gaatctttat	aaaaaacaag	agtgattgag	gcagattgta	240
aacattatta	aaaaacaaga	aacaaacaaa	aaaatagaga	aaaaaacac	cccaacacac	300
aa						302

&lt;210&gt; 256

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(301)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 256

gttccagaaa	acattgaagg	tggtttccca	aagtctaact	agggataccc	cctctagcct	60
aggaccctcc	tccccacacc	tcaatccacc	aaaccatcca	taatgcaccc	agataggccc	120
acccccaaaa	gcttgacac	cttgagcaca	cagttatgac	caggacagac	tcctctctat	180
aggcaaatag	ctgctggcaa	actggcatta	cctggtttgt	gggatgggg	gggcaagtgt	240
gtggcctctc	ggcctgggta	gcaagaacat	tcagggtagg	cctaagttan	tcgtgttagt	300
t						301

&lt;210&gt; 257

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

<400> 257							
gttgtggagg	aactctggct	tgctcattaa	gtcctactga	ttttcactat	ccctggaatt		60
tcccacttta	tttttgtctt	tcactatcgc	aggccttaga	agaggcttac	ctgcctccag		120
tottacctag	tccagttac	ccccggagt	tagaattgcc	atcctgaagt	gaaaagtaat		180
gtcacattac	tcccttcagt	gatttcttgt	agaagtgcc	atccctgaat	gccaccaaga		240
tcttaattct	cacatcttta	atcttatctc	tttgactcct	ctttacaccg	gagaaggctc		300
c							301

```
<210> 258
<211> 301
<212> DNA
<213> Homo sapien
```

```
<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G
```

<400> 258							
cagcagtagt	agatgccgta	tgccagcacg	cccagcactc	ccaggatcag	caccagcacc		60
agggggccag	ccaccaggcg	cagaagcaag	ataaacagta	ggctcaagac	cacagccacc		120
ccagggcaaa	caagaatcca	atacaggac	tgggcaaaat	cttcaagat	cttaacactg		180
atgtctcggg	cattgaggct	gtcaataana	cgctgatccc	ctgctgtatg	gtggtgtcat		240
tggatgatccc	tgggagcgcc	ggtggagtaa	cgttggtcca	tggaaagcag	cgcccacaac		300
t							301

```
<210> 259
<211> 301
<212> DNA
<213> Homo sapien
```

```
<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G
```

<400> 259						
tcatatatgc	aaacaaatgc	agactangcc	tcaggcagag	actaaaggac	atctottggg	60
gtgtcctgaa	gtgatttggg	cccctgaggg	cagacaccta	agtgggaatc	ccagtgggaa	120
gcaaagccat	aaggaagccc	aggattcctt	gtgatcagga	agtggccag	gaaggtctgt	180
tccagctcac	atctcatctg	catgcagcac	ggaccggatg	cgcccactgg	gtcttggtt	240
ccctcccatc	ttctcaagca	gtgtccttgt	tgagccattt	gcatccttgg	ctccaggtgg	300
c						301

```
<210> 260
<211> 301
<212> DNA
<213> Homo sapien
```

<400> 260						
ttttttttct	ccctaaggaa	aaagaaggaa	caagtctcat	aaaaccaa	aagcaatggt	60
aaggtgtctt	taactgaaaa	agattaggag	tcactggttt	acaagttata	attgaatgaa	120
agaactgtat	cagccacagt	tggccatttc	atgcgaatgg	cagcaaaaac	caggattaac	180
tagggcaaaa	taaataagtg	tgtggaagcc	ctgataagtg	cttaataaac	agactgattc	240
actgagacat	cagtacctgc	ccggggcgcc	gctcgagccg	aattctgcag	atatccatca	300
c						301

<210> 261  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 261  
 aaatattcga gcaaatcctg taactaatgt gtctccataa aaggctttga actcagtga 60  
 tctgcttcca tccacgattc tagcaatgac ctctcggaca tcaaagctcc tcttaagggt 120  
 agcaccaact attccataca attcatcagc aggaataaaa ggctcttcag aagggttcaat 180  
 ggtgacatcc aatttcttct gataatttag attcctcaca accttcctag ttaagtgaag 240  
 ggcattgatga tcatccaaag cccagtggtc acttactcca gactttctgc aatgaagatc 300  
 a 301

<210> 262  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 262  
 gaggagagcc tgttacagca tttgtaagca cagaatactc caggagtatt tgtaattgtc 60  
 tgtgagcttc ttgccgcaag tctctcagaa atttaaaaag atgcaaatcc ctgagtcacc 120  
 cctagacttc ctaaaccaga tcctctgggg ctggaacctg gcactctgca tttgtaatga 180  
 gggctttctg gtgcacacct aattttgtgc atctttgccc taaatcctgg attagtgtccc 240  
 catcattacc cccacattat aatgggatag attcagagca gatactctcc agcaaagaat 300  
 c 301

<210> 263  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 263  
 tttagcttgt ggtaatgac tcacaaaact gattttaaaa tcaagttaat gtgaattttg 60  
 aaaattacta cttaatccta attcacaata acaatggcat taaggtttga cttgagttgg 120  
 ttcttagtat tatttatggt aaataggctc ttaccacttg caaataactg gccacatcat 180  
 taatgactga cttcccagta aggtctctta aggggtaagt angaggatcc acaggatttg 240  
 agatgctaag gccccagaga tcgtttgatc caacctctt attttcagag gggaaaatgg 300  
 g 301

<210> 264  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 264  
 aaagacgtta aaccactcta ctaccacttg tggaactctc aaagggtaaa tgacaaaacc 60  
 aatgaatgac tctaaaaaca atatttacat ttaatgggtt gtagacaata aaaaaacaag 120  
 gtggatagat ctagaattgt aacattttta gaaaaccata scatttgaca gatgagaaag 180  
 ctcaattata gatgcaaaagt tataactaaa ctactatagt agtaaagaaa tacatttcac 240  
 acccttcata taaattcact atcttggtt gaggcactcc ataaaatgta tcacgtgcac 300  
 a 301

<210> 265



<211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 265  
 tgcccaagtt atgtgtaagt gtatccgcac ccagaggtaa aactacactg tcattcttgt 60  
 cttcttgtga cgcagtattt cttctctggg gagaagccgg gaagtcttct cctggctcta 120  
 catattcttg gaagtctcta atcaactttt gttccatttg ttctatttct tcaggaggga 180  
 ttttcagttt gtcaacatgt tctctaaca cacttgccca tttctgtaaa gaatccaaag 240  
 cagtccaagg ctttgacatg tcaacaacca gcataactag agtatccttc agagatacgg 300  
 c 301

<210> 266  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 266  
 taccgtctgc ccttcctccc atccaggcca tctgccaatc tacatgggtc ctcctattcg 60  
 acaccagatc actcttttct ctaccacag gcttgctatg agcaagagac acaacctcct 120  
 ctcttctgtg ttccagcttc ttttctgtt cttcccaccc ctttaagttct attcctgggg 180  
 atagagacac caatacccat aacctctctc ctaagcctcc ttataacca ggggtcacag 240  
 cacagactcc tgacaactgg taaggccaat gaactgggag ctcacagctg gctgtgcctg 300  
 a 301

<210> 267  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 267  
 aaagagcaca ggcagctca gcctgccctg gccatctaga ctcagcctgg ctccatgggg 60  
 gttctcagtg ctgagtcct ccaggaaaag ctcacctaga ccttctgagg ctgaatcttc 120  
 atcttcacag cgagcttctg agagcctgat attcctagcc ttgatgggtc ggagtaaagc 180  
 ctcattctga ttcctctcct tcttttctt caagttggct ttcctcacat ccctctgttc 240  
 aattcgcttc agcttgtctg ctttagccct catttcaga agcttcttct ctttggcatc 300  
 t 301

<210> 268  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 268  
 aatgtctcac tcaactactt ccagcctac cgtggcctaa ttctgggagt tttcttctta 60  
 gatcttggga gagctggttc ttctaaggag aaggagggaag gacagatgta actttggatc 120  
 tcgaagagga agtctaattg aagtaattag tcaacgggtc ttgttttagac tcttgggaata 180  
 tgctgggtgg ctcaagtgag ccttttgag aaagcaagta ttattottaa ggagtaacca 240  
 cttccatttg ttctactttc taccatcatc aattgtatat tatgtattct ttggagaact 300  
 a 301

<210> 269  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 269  
 taacaatata cactagctat ctttttaact gtccatcatt agcaccaatg aagattcaat 60

```

aaaattacct ttattcacac atctcaaaac aattctgcaa attcttagtg aagtttaact 120
atagtcacag accttaaata ttcacattgt tttctatgtc tactgaaaat aagttcacta 180
cttttctgga tattctttac aaaatcttat taaaattcct ggtattatca cccccaatta 240
tacagtagca caaccacctt atgtagtttt tacatgatag ctctgtagaa gtttcacatc 300
t 301

```

```

<210> 270
<211> 301
<212> DNA
<213> Homo sapien

```

```

<400> 270
cattgaagag cttttgcgaa acatcagaac acaagtgcct ataaaaattaa ttaagcctta 60
cacaagaata catattcctt ttattttctaa ggagttaaac atagatgtag ctgatgtgga 120
gagcttgctg gtgcagtgca tattggataa cactattcat ggccgaattg atcaagtcaa 180
ccaactcctt gaactggatc atcagaagaa gggtgggtgca cgatatactg cactagataa 240
tggaaccaacc aactaaattc tctcaccagg ctgtatcagt aaactggcctt aacagaaaac 300
a 301

```

```

<210> 271
<211> 301
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

```

```

<400> 271
aaaaggttct cataagatta acaatttaaa taaatatttg atagaacatt ctttctcatt 60
tttatagctc atcttttaggy ttgatattca gttcatgcct cccttgctgt tcttgatcca 120
gaattgcaat cacttcatca gcctgtattc gctccaattc tctataaagt ggggtccaagg 180
tgaaccacag agccacagca cacctctttc ccttgggtgac tgccttcacc ccatganggt 240
tctctctccc agatganaac tgatcatgcy cccacatttt gggttttata gaagcagtca 300
c 301

```

```

<210> 272
<211> 301
<212> DNA
<213> Homo sapien

```

```

<400> 272
taaattgcta agccacagat aacaccaatc aaatggaaca aatcactgtc ttcaaagtgc 60
ttatcagaaa accaaatgag cctggaatct tcataatacc taaacatgcc gtatttagga 120
tccaataatt ccctcatgat gagcaagaaa aattctttgc gcaccctcc tgcattccaca 180
gcatcttctc caacaaatat aaccttgagt ggcttctgtt aatctatgtt ctttgttttc 240
ctaaggactt ccattgcac tcctacaata ttttctctac gcaccactag aattaagcag 300
g 301

```

```

<210> 273
<211> 301
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(301)

```

<223> n = A,T,C or G

<400> 273

acatgtgtgt atgtgtatct ttgggaaan aanaagacat cttgtttayt atttttttgg	60
agagangctg ggacatggat aatcacwtaa ttgtctayta tyactttaat ctgactygaa	120
gaaccgtcta aaaataaaat ttaccatgtc dtatatctct tatagtatgc ttatttcacc	180
tttcttctgt ccagagagag tatcagtgac ananatttma ggggtgaamac atgmattggg	240
gggacttnty tttacngagm accctgcccg sgcgcctcgc makcngantt ccgcsananc	300
t	301

<210> 274

<211> 301

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(301)

<223> n = A,T,C or G

<400> 274

cttatatact ctttctcaga ggcaaaagag gagatgggta atgtagacaa ttctttgagg	60
aacagtaaatt gattattaga gagaangaat ggaccaagga gacagaaatt aacttgtaaa	120
tgattctctt tggaatctga atgagatcaa gaggccagct ttagcttggt gaaaagtcca	180
tctagggtat gttgcattct cgtcttcttt tctgcagtag ataatgaggt aaccgaaggc	240
aattgtgctt cttttgataa gaagctttct tggtcataac aggaaattcc aganaaagtc	300
c	301

<210> 275

<211> 301

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(301)

<223> n = A,T,C or G

<400> 275

tcggtgtcag cagcacgtgg cattgaacat tgcaatgtgg agcccaaacc acagaaaatg	60
gggtgaaatt ggccaacttt ctattaactt atgttggcaa ttttgccacc aacagtaagc	120
tgcccttctt aataaaagaa aattgaaaagg tttctcacta aacggaatta agtagtggag	180
tcaagagact cccaggcctc agcgtacctg cccgggcggc cgctcgaagc cgaattctgc	240
agatatccat cacactggcg gncgctcgan catgcatcta gaaggnccaa ttcgccctat	300
a	301

<210> 276

<211> 301

<212> DNA

<213> Homo sapien

<400> 276

tgtacacata ctcaataaat aaatgactgc attgtggat tattactata ctgattatat	60
ttatcatgtg acttctaatt agaaaatgta tccaaaagca aaacagcaga tatacaaaat	120
taagagaca gaagatagac attaacagat aaggcaactt atacattgag aatccaaatc	180
caatacattt aaacatttgg gaaatgaggg ggacaaatgg aagccagatc aaatttgtgt	240
aaaactatc agtatgtttc cttgtcttca tgtctgagaa ggctctcctt caatggggat	300
g	301

<210> 277  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 277  
 tttgttgatg tcagtatttt attacttgcg ttatgagtgc tcacctggga aattctaaag 60  
 atacagagga cttggaggaa gcagagcaac tgaatttaat ttaaaagaag gaaaacattg 120  
 gaatcatggc actcctgata ctttcccaaa tcaacactct caatgcccc ccctcgtcct 180  
 caccatagtg gggagactaa agtggccacg gatttgcctt angtgtgcag tgcgttctga 240  
 gttcnctgtc gattacatct gaccagtctc ctttttccga agtcctntccg ttcaatcttg 300  
 c 301

<210> 278  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 278  
 taccactaca ctccagcctg ggcaacagag caagacctgt ctcaaagcat aaaatggaat 60  
 aacatatcaa atgaaacagg gaaaatgaag ctgacaattt atggaagcca gggcttgta 120  
 cagtctctac tgttattatg cattacctgg gaatttatat aagcccttaa taataatgcc 180  
 aatgaacatc tcatgtgtgc tcacaatggt ctggcactat tataagtgtc tcacagggtt 240  
 tatgtgttct tcgtaacttt atggantagg tactcggccg cgaacacgct aagccgaatt 300  
 c 301

<210> 279  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 279  
 aaagcaggaa tgacaaagct tgcttttctg gtatgttcta ggtgtattgt gacttttact 60  
 gttatattaa ttgccaatat aagtaaata agattatata tgtatagtgt ttcacaaagc 120  
 ttagaccttt acctccagc caccacacag tgcttgatat ttcagagtca gtcattgggt 180  
 atacatgtgt agttccaaag cacataagct agaanaanaa atatttctag ggagcactac 240  
 catctgtttt cacatgaaat gccacacaca tagaactcca acatcaattt cattgcacag 300  
 a 301

<210> 280  
 <211> 301  
 <212> DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 280

ggtactggag	ttttcctccc	ctgtgaaaac	gtaactactg	ttgggagtga	attgaggatg	60
tagaaagggtg	gtggaaccaa	attgtgggtca	atggaaatag	gagaatatgg	ttctcactct	120
tgagaaaaaa	acctaagatt	agcccaggta	gttgccctgta	acttcagttt	ttctgcctgg	180
gtttgatata	gtttagggtt	ggggtttagat	taagatctaa	attacatcag	gacaaagaga	240
cagactatta	actccacagt	taattaagga	ggtatgttcc	atgtttat	gttaaagcag	300
t						301

&lt;210&gt; 281

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 281

aggtacaaga	aggggaatgg	gaaagagctg	ctgctgtggc	attgttcaac	ttggatat	60
gccgagcaat	ccaaatcctg	aatgaagggg	catcttctga	aaaaggagat	ctgaatctca	120
atgtggtagc	aatggcttta	tcgggttata	cggatgagaa	gaactccctt	tgagagagaa	180
tggttagcac	actgcgatta	cagctaaata	acccgtat	gtgtgtcatg	tttgcatttc	240
tgacaagtga	aacaggatct	tacgatggag	ttttgtatga	aaacaaagtt	gcagtacctc	300
g						301

&lt;210&gt; 282

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 282

caggtactac	agaattaaaa	tactgacaag	caagtagttt	cttggcgtgc	acgaattgca	60
tcagaacccc	aaaaattaag	aaattcaaaa	agacattttg	tgggcacctg	ctagcacaga	120
agcgcagaag	caaagccag	gcagaacat	gctaacctta	cagctcagcc	tgacacagaag	180
cgagaagca	aagcccagc	agaaccatgc	taaccttaca	gctcagcctg	cacagaagcg	240
cagaagcaaa	gccaggcgag	aacatgctaa	ccttacagct	cagcctgcac	agaagcacag	300
a						301

&lt;210&gt; 283

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 283

atctgtatac	ggcagacaaa	ctttatarag	tgtagagagg	tgagcgaaag	gatgcaaaag	60
cactttgagg	gctttataat	aatatgctgc	ttgaaaaaaa	aaatgtgtag	ttgatactca	120
gtgcatctcc	agacatagta	aggggttgct	ctgaccaatc	aggtgatcat	tttttctatc	180
acttcccagg	ttttatgcaa	aaatttgtt	aaattctata	atggtgat	gcatctttta	240
ggaaacatat	acatttttta	aaatctat	tatgtaagaa	ctgacagacg	aatttgcttt	300
g						301

&lt;210&gt; 284

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 284

caggtacaaa	acgctattaa	gtggcttaga	atttgaacat	ttgtggctct	tatttacttt	60
gcttcgtgtg	tgggcaaagc	aacatcttcc	ctaaatata	attaccaaga	aaagcaagaa	120
gcagattagg	tttttgacaa	aacaaacag	ccaaaagggg	gctgacctgg	agcagagcat	180

93

```

ggtgagagggc aaggcatgag agggcaagtt tgttgtggac agatctgtgc ctactttatt 240
actggagtaaa aagaaaacaa agttcattga tgtcgaagga tatataacagt gttagaaatt 300
a                                                                 301

```

```

<210> 285
<211> 301
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)... (301)
<223> n = A,T,C or G

```

```

<400> 285
acatcacccat gatcggtatcc cccacccatt atacgttgta tgtttacata aatactcttc 60
aatgatcatt agtgttttaa aaaaaatact gaaaactcct tctgcatccc aatctctaac 120
caggaaagca aatgctattt acagacctgc aagccctccc tcaaacnaaa ctatttctgg 180
attaaatatg tctgacttct tttgaggtca cactgactag caaatgctat ttacgatctg 240
caaaagctgt ttgaagagtc aaagcccca tgtgaacacg atttctggac cctgtaacag 300
t                                                                 301

```

```

<210> 286
<211> 301
<212> DNA
<213> Homo sapien

```

```

<400> 286
taccactgca ttccagcctg ggtgacagag tgagactccg tctccaaaaa aaactttgct 60
tgtatatatt ttttgcctta cagtggatca ttctagtagg aaaggacagt aagatttttt 120
atcaaaatgt gtcatgccag taagagatgt tatattcttt tctcatttct tccccacca 180
aaaataagct accatatagc ttataagtct caaatttttg ctttttacta aaatgtgatt 240
gtttctgttc attgtgtatg cttcatcacc tatattagc aaattccatt ttttcccttg 300
t                                                                 301

```

```

<210> 287
<211> 301
<212> DNA
<213> Homo sapien

```

```

<400> 287
tacagatctg ggaactaaat attaaaaatg agtgtggctg gatatatgga gaatgttggg 60
cccagaagga acgtagagat cagatattac aacagctttg ttttgagggg tagaaatatg 120
aaatgatttg gttatgaacg cacagtttag gcagcagggc cagaatcctg accctctgcc 180
ccgtggttat ctctcctcca gcttggctgc ctcatgttat cacagtattc cattttgttt 240
gttgcattgc ttgtgaagcc atcaagattt tctcgtctgt tttcctctca ttggtaatgc 300
t                                                                 301

```

```

<210> 288
<211> 301
<212> DNA
<213> Homo sapien

```

```

<400> 288
gtacacctaa ctgcaaggac agctgaggaa tgtaatgggc agccgctttt aaagaagtag 60
agtcaatagg aagacaaatt ccagttccag ctcagtctgg gtatctgcaa agctgcaaaa 120
gatctttaaa gacaatttca agagaatatt tccttaaagt tggcaatttg gagatcatac 180
aaaagcatct gcttttgtga ttttaatttag ctcatctggc cactggaaga atccaaacag 240

```

94

tctgccttaa ttttgatga atgcatgatg gaaattcaat aatttagaaa gttaaaaaaa 300  
a 301

<210> 289  
<211> 301  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(301)  
<223> n = A,T,C or G

<400> 289  
ggtacactgt ttccatgtta tgtttctaca cattgctacc tcagtgtccc tggaaactta 60  
gctttttagtg tctccaagta gtccaccttc atttaactct ttgaaactgt atcatctttg 120  
ccaagtaaga gtggtggcct atttcagctg ctttgacaaa atgactggct cctgacttaa 180  
cgtttotataa atgaatgtgc tgaagcaaag tgcccatggt ggcggcgaan aagagaaaga 240  
tgtgttttgt tttggactct ctgtggtccc ttccaatgct gtgggtttcc aaccagnnga 300  
a 301

<210> 290  
<211> 301  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(301)  
<223> n = A,T,C or G

<400> 290  
acactgagct cttcttgata aatatacaga atgcttggca tatacaagat tctatactac 60  
tgactgatct gttcatttct ctacagctc ttaccccaa agcttttcc accctaagtg 120  
ttctgacctc cttttctaata cacagtaggg atagaggcag anccacctac aatgaacatg 180  
gagttctatc aagaggcaga aacagcacag aatcccagtt ttaccattcg ctgacagtgc 240  
tgccttgaac aaaaacattt ctccatgtct cattttcttc atgcctcaag taacagttag 300  
a 301

<210> 291  
<211> 301  
<212> DNA  
<213> Homo sapien

<400> 291  
caggtagcaa tttcttctat cctagaaaca tttcatttta tgttgttgaa acataacaac 60  
tatatcagct agattttttt tctatgcttt acctgctatg gaaaatttga cacattctgc 120  
tttactcttt tgtttatagg tgaatcacia aatgtatttt tatgtattct gtagttcaat 180  
agccatggct gtttacttca ttttaatttat ttagcataaa gacattatga aaaggcctaa 240  
acatgagctt cacttcccca ctaactaatt agcatctgtt atttcttaac cgtaatgcct 300  
a 301

<210> 292  
<211> 301  
<212> DNA  
<213> Homo sapien

<220>

<221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 292  
 accttttagt agtaatgtct aataataaat aagaaatcaa ttttataagg tccatatagc 60  
 tgtattaaat aatttttaag tttaaaagat aaaataccat catttttaaat gttggtattc 120  
 aaaaccaaag natataaccg aaaggaaaaa cagatgagac ataaaatgat ttgcnagatg 180  
 ggaaatatag tasttyatga atgttnatta aattccagtt ataatagtgg ctacacactc 240  
 tctactacaca cacagacccc acagtccctat atgccacaaa cacattttcca taacttgaaa 300  
 a 301

<210> 293  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 293  
 ggtaccaagt gctgggtgcc gctgtttacc tgtttctact gaaaagtctg gctaattgctc 60  
 ttgtgtagtc acttctgatt ctgacaatca atcaatcaat ggcctagagc actgactgtt 120  
 aacacaaacg tctactagcaa agtagcaaca gctttaagtc taaatacaaa gctgtttctgt 180  
 gtgagaattt tttaaaaggc tacttgtata ataacccttg tcattttttaa tgtacctcgg 240  
 ccgcgaccac gctaagccga attctgcaga tatccatcac actggcgggc gctcgagcat 300  
 g 301

<210> 294  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 294  
 tgacccataa caatatacac tagctatctt tttaactgtc catcattagc accaatgaag 60  
 attcaataaa attaccctta ttcacacatc tcaaaaacaat tctgcaaatt cttagtgaag 120  
 tttaactata gtcacaganc ttaaattatc acattgtttt ctatgtctac tgaaaataag 180  
 ttcactactt ttctgggata ttctttacaa aatcttatta aaattcctgg tattatcacc 240  
 cccaattata cagtagcaca accacottat gtagttttta catgatagct ctgtagaggt 300  
 t 301

<210> 295  
 <211> 305  
 <212> DNA  
 <213> Homo sapien

<400> 295  
 gtactctttc tctcccctcc tctgaattta attctttcaa cttgcaattt gcaaggatta 60  
 cacatttcac tgtgatgtat attgtgttgc aaaaaaaaaa gtgtctttgt ttaaaattac 120  
 ttggtttgtg aatccatctt gctttttccc cattggaact agtcattaac ccatctctga 180  
 actggtagaa aaacrtctga agagctagtc tatcagcatc tgacagggtga attggatgg 240  
 tctcagaacc atttcaccca gacagcctgt ttctatcctg ttttaataaat tagtttgggt 300  
 tctct 305

<210> 296  
 <211> 301



<212> DNA  
 <213> Homo sapien

<400> 296  
 aggtactatg ggaagctgct aaaataatat ttgatagtaa aagtatgtaa tgtgctatct 60  
 cacctagtag taaactaaaa ataaactgaa actttatgga atctgaagtt attttccttg 120  
 attaaataga attaataaac caatatgagg aaacatgaaa ccatgcaatc tactatcaac 180  
 tttgaaaaag tgattgaacg aaccacttag ctttcagatg atgaacactg ataagtcatt 240  
 tgtcattact ataaatttta aaatctgtta ataagatggc ctataggag gaaaaagggg 300  
 c 301

<210> 297  
 <211> 300  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(300)  
 <223> n = A,T,C or G

<400> 297  
 actgagtttt aactggacgc caagcaggca aggctggaag gttttgctct ctttgtgcta 60  
 aagggtttga aaaccttgaa ggagaatcat ttgacaaga agtacttaag agtctagaga 120  
 acaaagangt gaaccagctg aaagctctcg ggggaanctt acatgtgttg ttaggcctgt 180  
 tccatcattg ggaagtgcact ggccatccct caaaatttgt ctgggctggc ctgagtggtc 240  
 accgcacctc ggccgcgacc acgctaagcc gaattctgca gatatccatc acactggcgg 300

<210> 298  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 298  
 tatggggttt gtcacccaaa agctgatgct gagaaaggcc tccctggggc ccctcccgcg 60  
 ggcattctgag agacctggtg ttccagtgtt tctggaaatg ggtcccagtg ccgcccggctg 120  
 tgaagctctc agatcaatca cgggaaggcg ctggcggtgg tggccacctg gaaccaccct 180  
 gtccctgtctg ttacatttc actaycaggt tttctctggg cattacnatt tgttccccta 240  
 caacagtgcac ctgtgcattc tgctgtggcc tgctgtgtct gcaggtggct ctacgcgagg 300  
 t 301

<210> 299  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 299  
 gttttgagac ggagttttcac tcttgttgcc cagactggac tgcaatggca gggctctctgc 60  
 tcaactgcacc ctctgcctcc caggttcgag caattctcct gcctcagcct ccaggttagc 120  
 tgggattgca ggctcacgcc accataccca gctaattttt ttgtattttt agtagagacg 180  
 gaggtttcgcc atgttggccca gctgggtctca aactcctgac ctcaagcgac ctgcctgcct 240  
 cggcctccca aagtgtctga attataggca tgagtcaaca cgcccagcct aaagatattt 300  
 t 301

<210> 300  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 300  
 attcagtttt atttgctgcc ccagtatctg taaccaggag tgccacaaaa tcttgccaga 60  
 tatgtccac acccactggg aaaggctccc acctggctac ttctctatc agctgggtca 120  
 gctgcattcc acaaggttct cagcctaatt agtttcaacta cctgccagtc tcaaaactta 180  
 gtaaagcaag accatgacat tccccacgg aaatcagagt ttgccccacc gtcttggtac 240  
 tataaagcct gcctctaaca gtccttgctt cttcacacca atcccgagcg catcccccat 300  
 g 301

<210> 301  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 301  
 tttaaatttt gagaggataa aaaggacaaa taatctagaa atgtgtcttc ttcagtctgc 60  
 agaggacccc aggtctccaa gcaaccacat ggtcaagggc atgaataatt aaaagttggt 120  
 gggaactcac aaagaccctc agagctgaga caccacacaac agtgggagct cacaagacc 180  
 ctgagagctg agacaccac aacagtggga gctcacaag accctcagag ctgagacacc 240  
 cacaacagca cctcgttcag ctgccacatg tgtgaataag gatgcaatgt ccagaagtgt 300  
 t 301

<210> 302  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 302  
 aggtacacat ttagcttggt gtaaatgact cacaaaaactg attttaaaat caagttaatg 60  
 tgaattttga aaattactac ttaatcctaa ttcacaataa caatggcatt aaggtttgac 120  
 ttgagttggt tcttagtatt atttatggtt aataggctct taccacttgc aaataactgg 180  
 ccacatcatt aatgactgac ttcccagtaa ggctctctaa ggggtaagta ggaggatcca 240  
 caggatttga gatgctaagg ccccagagat cgtttgatcc aaccctctta ttttcagagg 300  
 g 301

<210> 303  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 303  
 aggtaccaac tgtggaaata ggtagaggat ctttttttct ttccatatca actaagttgt 60  
 atattgtttt ttgacagttt aacacatctt cttctgtcag agatttcttc acaatagcac 120  
 tggctaattg aactaccgct tgcattgtaa aaatgggtgt ttgtgaaatg atcataggcc 180  
 agtaacgggt atgtttttct aactgatctt ttgctcgttc caaagggacc tcaagacttc 240  
 catcgatttt atatctgggg tctagaaaag gagttaatct gttttccctc ataaattcac 300  
 c 301

<210> 304  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

&lt;400&gt; 304

```

acatggatgt tattttgcag actgtcaacc tgaatttgta tttgcttgac attgcctaatt      60
tattagtttc agtttcagct taccactttt ttgtctgcaa catgcaraas agacagtgcc      120
cttttttagtg tatcatatca ggaatcatct cacattgggtt tgtgccatta ctgggtgcagt      180
gacttttcagc cacttgggta aggtggagtt ggccatatgt ctccactgca aaattactga      240
ttttcctttt gtaattaata agtgtgtgtg tgaagattct ttgagatgag gtatatatct      300
c                                                                    301

```

&lt;210&gt; 305

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)... (301)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 305

```

gangtacagc gtggtcaagg taacaagaag aaaaaaatgt gagtggcatc ctgggatgag      60
cagggggaca gacctggaca gacacgttgt catttgctgc tgtgggtagg aaaatgggag      120
taaaggagga gaaacagata caaaatctcc aactcagtat taaggatttc tcatgcctag      180
aatattggtg gaaacaagaa tacattcata tggcaaataa ctaaccatgg tggaacaaaa      240
ttctgggatt taagttggat accaangaaa ttgtattaaa agagctgttc atggaataag      300
a                                                                    301

```

&lt;210&gt; 306

&lt;211&gt; 8

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 306

```

Val Leu Gly Trp Val Ala Glu Leu
1           5

```

&lt;210&gt; 307

&lt;211&gt; 637

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 307

```

acaggggratg aagggaaagg gagaggatga ggaagcccc ctggggattt ggtttgggtcc      60
ttgtgatcag gtggtctatg gggcttatcc ctacaaagaa gaatccagaa atagggggcac      120
attgaggaat gatacttgag cccaaagagc attcaatcat tgttttattt gccttmtttt      180
cacaccattg gtgagggagg gattaccacc ctgggggttat gaagatgggtt gaacacccca      240
cacatagcac cggagatatg agatcaacag tttcttagcc atagagattc acagcccaga      300
gcaggaggac gcttgcacac catgcaggat gacatggggg atgcgctcgg gattgggtgtg      360
aagaagcaag gactgttaga ggcaggcttt atagtaacaa gacggtgggg caaactctga      420
tttccgtggg ggaatgtcat ggtcttgctt tactaagttt tgagactggc aggtagtga      480
actcattagg ctgagaacct tgtggaatgc acttgaccca sctgatagag gaagtagcca      540
ggtgggagcc tttcccagtg ggtgtgggac atatctggca agattttgtg gcactcctgg      600
ttacagatac tggggcagca aataaaaactg aatcttg                                                                    637

```

&lt;210&gt; 308

&lt;211&gt; 647

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

99

<220>  
 <221> misc\_feature  
 <222> (1)...(647)  
 <223> n = A,T,C or G

<400> 308  
 acgattttca ttatcatgta aatcgggtca ctcaaggggc caaccacagc tgggagccac 60  
 tgctcagggg aaggttcata tgggactttc tactgcccac gggtctatac aggatataaa 120  
 gngcctcac agtatagatc tggtagcaaa gaagaagaaa caaacactga tctctttctg 180  
 ccacccctct gacccttttg aactcctctg accctttaga acaagcctac ctaatatctg 240  
 ctagagaaaa gaccaacaac ggcctcaaag gatctcttac catgaaggtc tcagctaatt 300  
 cttggctaag atgtgggttc cacattaggt tctgaatatg gggggaagg tcaatttgct 360  
 cattttgtgt gtggataaag tcaggatgcc caggggccag agcagggggc tgcttgcttt 420  
 ggaacaatg gctgagcata taaccatagg ttatggggaa caaaacaaca tcaaagtcac 480  
 tgatatcaatt gccatgaaga cttgagggac ctgaatctac cgattcatct taaggcagca 540  
 ggaccagttt gagtggcaac aatgcagcag cagaatcaat ggaaacaaca gaatgattgc 600  
 aatgtccttt tttttctcct gcttctgact tgataaaagg ggaccgt 647

<210> 309  
 <211> 460  
 <212> DNA  
 <213> Homo sapien

<400> 309  
 actttatagt ttaggctgga cattggaaaa aaaaaaaagc cagaacaaca tgtgatagat 60  
 aatatgattg gctgcacact tccagactga tgaatgatga acgtgatgga ctattgtatg 120  
 gagcacatct tcagcaagag ggggaaatac tcatcatttt tggccagcag ttgtttgatc 180  
 accaaacatc atgccagaat actcagcaaa ccttcttagc tcttgagaag tcaaagtccg 240  
 ggggaattta ttccctggcaa ttttaattgg actccttatg tgagagcagc ggctaccag 300  
 ctgggggtgt ggagcgaacc cgtcactagt ggacatgcag tggcagagct cctggtaacc 360  
 acctagagga atacacaggc acatgtgtga tgccaagcgt gacacctgta gcactcaaat 420  
 ttgtcttgtt tttgtctttc ggtgtgtaag attcttaagt 460

<210> 310  
 <211> 539  
 <212> DNA  
 <213> Homo sapien

<400> 310  
 acgggactta tcaataaaag ataggaaaag aagaaaactc aaatattata ggcagaaatg 60  
 ctaaaggttt taaaatatgt caggattgga agaaggcatg gataaagaac aaagttcagt 120  
 taggaaagag aaacacagaa ggaagagaca caataaaagt cattatgtat tctgtgagaa 180  
 gtcagacagt aagatttggt ggaatgggt tggtttggtg tatggtatgt attttagcaa 240  
 taatctttat ggcagagaaa gctaaaatcc ttttagcttg gtgaatgatc acttgctgaa 300  
 ttctcaagg taggcatgat gaaggagggt ttagaggaga cacagacaca atgaactgac 360  
 ctatagataga agccttagta tactcagcta ggaatagtga ttctgagggc aactgtgac 420  
 atgattatgt cattacatgt atggtagtga tggggatgat aggaaggaag aacttatggc 480  
 atattttcac cccacaaaa gtcagttaaa tattgggaca ctaaccatcc aggtcaaga 539

<210> 311  
 <211> 526  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(526)  
 <223> n = A,T,C or G

100

```

<400> 311
caaatttgag ccaatgacat agaattttac aaatcaagaa gcttattctg gggccatttc      60
ttttgacgtt ttctctaaac tactaaagag gcattaatga tccataaatt atattatcta      120
catttacagc atttaaaatg tgttcagcat gaaatattag ctacagggga agctaaataa      180
attaaacatg gaataaagat ttgtccttaa atataatcta caagaagact ttgatatttg      240
tttttcacaa gtgaagcatt cttataaagt gtcataacct ttttggggaa actatgggaa      300
aaaatgggga aactctgaag ggttttaagt atcttacctg aagctacaga ctccataacc      360
tctctttaca gggagctcct gcagccccta cagaaatgag tggctgagat tcttgattgc      420
acagcaagag cttctcatct aaaccctttc cctttttagt atctgtgtat caagtataaa      480
agttctataa actgtagtnt acttatttta atcccaaaag cacagt                      526

```

&lt;210&gt; 312

&lt;211&gt; 500

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(500)

&lt;223&gt; n = A,T,C or G

```

<400> 312
cctctctctc cccaccccct gactctagag aactggggtt tctcccagta ctccagcaat      60
tcattttctga aagcagttga gccactttat tccaaagtac actgcagatg ttcaaactct      120
ccattttctct ttcccttcca cctgccagtt ttgctgactc tcaacttgct atgagtgtaa      180
gcattaagga cattatgctt cttcgattct gaagacaggc cctgctcatg gatgactctg      240
gcttcttagg aaaatatttt tcttccaaaa tcagtaggaa atctaaactt atccctctct      300
tgcagatgtc tagcagcttc agacatttgg ttaagaacct atgggaaaaa aaaaaatcct      360
tgctaattgtg gtttcctttg taaaccanga ttcttatttg nctggtatag aatatcagct      420
ctgaacgtgt ggtaaagatt tttgtgtttg aatataggag aaatcagttt gctgaaaagt      480
tagtcttaat tatctatttg                                     500

```

&lt;210&gt; 313

&lt;211&gt; 718

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(718)

&lt;223&gt; n = A,T,C or G

```

<400> 313
ggagatttgt gtggttttga gccgaggag accaggaaga tctgcatggt gggaaggacc      60
tgatgataca gaggtgagaa ataagaaagg ctgctgactt taccatctga ggccacacat      120
ctgctgaaat ggagataatt aacatcacta gaaacagcaa gatgacaata taatgtctaa      180
gtagtacat gtttttgac atttccagcc cttttaaata tccacacaca caggaagcac      240
aaaagggaagc acagagatcc ctgggagaaa tgcccggccg ccatcttggg tcatcgatga      300
gcctcgccct gtgcctgntc ccgcttgtga gggaggaca ttagaaaatg aattgatgtg      360
ttccttaaaag gatggcagga aaacagatcc tgttgtggat atttatttga acgggattac      420
agatttgaaa tgaagtcaca aagtgcacat taccaatgag aggaaaacag acgagaaaat      480
cttgatggtt cacaagacat gcaacaaaca aaatggaata ctgtgatgac acgagcagcc      540
aactggggag gagataccac ggggcagagg tcaggattct ggccctgctg cctaactgtg      600
cgttatacca atcatttcta tttctaccct caaacaagct gtngaataac tgacttacgg      660
ttcttntggc ccacatttct atnatccacc cctccttttt aannttantc caaantgt      718

```

&lt;210&gt; 314

101

<211> 358  
 <212> DNA  
 <213> Homo sapien

<400> 314  
 gtttatttac attacagaaa aaacatcaag acaatgtata ctatttcaaa tatatccata 60  
 cataatcaaa tatagctgta gtacatgttt tcattgggtg agattaccac aaatgcaagg 120  
 caacatgtgt agatctcttg tcttattctt ttgtctataa tactgtattg tgtagtccaa 180  
 gctctcggta gtccagccac tgtgaacat gctcccttta gattaacctc gtggacgctc 240  
 ttgttgatt gctgaactgt agtgcctgt attttgcttc tgtctgtgaa ttctgttget 300  
 tctggggcat ttccttgta tgcagaggac caccacacag atgacagcaa tctgaatt 358

<210> 315  
 <211> 341  
 <212> DNA  
 <213> Homo sapien

<400> 315  
 taccacctcc ccgtggcac tgatgagccg catcaccatg gtcaccagca ccatgaaggc 60  
 ataggatg atgaggacat ggaatgggcc cccaaggatg gtctgtccaa agaagcgagt 120  
 gaccccatc ctgaagatgt ctggaacctc taccagcagg atgatgatag ccccaatgac 180  
 agtcaccagc tccccagca gccggatc gtccttaggg gtcatttagg cttcctgaag 240  
 tagcttctgc tgtaagaggg tggtgtcccg ggggctcgtg cggttattgg tctgggctt 300  
 gagggggcgg tagatgcagc acatggtgaa gcagatgatg t 341

<210> 316  
 <211> 151  
 <212> DNA  
 <213> Homo sapien

<400> 316  
 agactgggca agactcttac gcccacact gcaatttggt cttgttgccg tatccattta 60  
 tgtgggcctt tctcgagttt ctgattataa acaccactgg agcgatgtgt tgactggact 120  
 catcaggga gctctggttg caatattagt t 151

<210> 317  
 <211> 151  
 <212> DNA  
 <213> Homo sapien

<400> 317  
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 ccagggtctt gttcttgcca cacctgcttg a 151

<210> 318  
 <211> 151  
 <212> DNA  
 <213> Homo sapien

<400> 318  
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 tgggggcgtt ttatcaggca gtgataaaca t 151

<210> 319  
 <211> 151  
 <212> DNA

102

&lt;213&gt; Homo sapien

&lt;400&gt; 319

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taagattggg	tttatgtgat	tttagtgggt	a			151

&lt;210&gt; 320

&lt;211&gt; 150

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 320

aactagtggg	tccactagtc	cagtgtgggtg	gaattccatt	gtgttgggggt	tctagatcgc	60
gagcggctgc	cctttttttt	tttttttttg	ggggggaatt	tttttttttt	aatagtatt	120
gagtgttcta	cagcttacag	taaataccat				150

&lt;210&gt; 321

&lt;211&gt; 151

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 321

agcaactttg	tttttcatcc	aggttatfff	aggcttagga	tttcctctca	caactgcagtt	60
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tgctctgag	aaatcaaagt	cttcatacac	t			151

&lt;210&gt; 322

&lt;211&gt; 151

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(151)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 322

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attgtgcagg	gctcgttca	nacttccagt	t			151

&lt;210&gt; 323

&lt;211&gt; 151

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(151)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 323

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nagactcant	tactaccacg	tttgtgggtt	twtgaggagaa	atgtaactgg	acagttagct	120
gttcaatyaa	aaagacactt	ancccatgtg	g			151

&lt;210&gt; 324

103

<211> 461  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(461)  
 <223> n = A,T,C or G

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 agagttacta cgaatcccat cttgggtcca gctatatcac tgacagcatg gtagaagact 180  
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 ctcatcacgg gatatacaaaa taccctttgt gctacccagg ccctggggaa tcaggtgact 300  
 cacacaaaatg caatagtttg tcaactgcatt tttacctgaa ccaaagctaa acccggtgtt 360  
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 aaaaacgcac aagagcccct gccctgccct agctgangca c 461

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 <212> DNA  
 <213> Homo sapien

<400> 325  
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 agtaagagtg gtggcctatt tcagctgctt tgacaaaaatg actggctcct gacttaacgt 180  
 tctataaatg aatgtgctga agcaaagtgc ccatgggtggc ggcaagaag agaaagatgt 240  
 gttttgtttt ggactctctg tggcccttc caatgctgtg gggttccaac caggggaagg 300  
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 <211> 1215  
 <212> DNA  
 <213> Homo sapien

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104

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 aaaaaaaaaa aaaaaa 1215

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 <211> 220  
 <212> PRT  
 <213> Homo sapien

<400> 327  
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 20 25 30  
 Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu Gly  
 35 40 45  
 Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val Glu  
 50 55 60  
 Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu Leu Ala  
 65 70 75 80  
 Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser Asp  
 85 90 95  
 Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly Asn  
 100 105 110  
 Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg Met Pro  
 115 120 125  
 Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu Glu Val Cys  
 130 135 140  
 Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys Ala Gly  
 145 150 155 160  
 Gly Gly Gln Asp Gln Lys Asp Ser Cys Asn Gly Asp Ser Gly Gly Pro  
 165 170 175  
 Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly Lys Ala  
 180 185 190  
 Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn Leu Cys Lys  
 195 200 205  
 Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser  
 210 215 220

<210> 328  
 <211> 234  
 <212> DNA  
 <213> Homo sapien

<400> 328  
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 atccgcagtg ggtgctgtca gccacacact gttccagaa ctctacacc atcgggctgg 180  
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<210> 329  
 <211> 77  
 <212> PRT  
 <213> Homo sapien

<400> 329  
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105

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Phe	Cys	Ser	Gly	Val	Leu	Val	His	Pro	Gln	Trp	Val	Leu	Ser	Ala	Thr
	35						40					45			
His	Cys	Phe	Gln	Asn	Ser	Tyr	Thr	Ile	Gly	Leu	Gly	Leu	His	Ser	Leu
	50					55					60				
Glu	Ala	Asp	Gln	Glu	Pro	Gly	Ser	Gln	Met	Val	Glu	Ala			
65					70				75						

<210> 330  
 <211> 70  
 <212> DNA  
 <213> Homo sapien

<400> 330  
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 gctgcagcca 70

<210> 331  
 <211> 22  
 <212> PRT  
 <213> Homo sapien

	20		25		30										
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1			5				10					15			
Val	Ser	Gly	Ser	Cys	Ser										
	20														

<210> 332  
 <211> 2507  
 <212> DNA  
 <213> Homo sapien

<400> 332

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gcttcttagc	tgaggaaaaag	cacctccacg	ttttgatcaa	caatgcagga	gtgatgatgt	420
gtccgtactc	gaagacagca	gatggctttg	agatgcacat	aggagtcaac	cacttgggtc	480
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 <213> Homo sapien

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<210> 334  
 <211> 2417  
 <212> DNA  
 <213> Homo sapien

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&lt;211&gt; 2984

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 335

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 Pro Lys Gln Pro Gln Lys Arg Ser Arg Ala Ala Phe Ser His Thr Gln  
 35 40 45  
 Val Ile Glu Leu Glu Arg Lys Phe Ser His Gln Lys Tyr Leu Ser Ala  
 50 55 60  
 Pro Glu Arg Ala His Leu Ala Lys Asn Leu Lys Leu Thr Glu Thr Gln  
 65 70 75 80  
 Val Lys Ile Trp Phe Gln Asn Arg Arg Tyr Lys Thr Lys Arg Lys Gln  
 85 90 95  
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 100 105 110  
 Leu Lys Glu Glu Ala Phe Ser Arg Ala Ser Leu Val Ser Val Tyr Asn  
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Cys Thr Ser Thr Val Gln Leu Pro Gly Lys Val Val Val Val Thr Gly  
35 40 45  
Ala Asn Thr Gly Ile Gly Lys Glu Thr Ala Lys Glu Leu Ala Gln Arg  
50 55 60  
Gly Ala Arg Val Tyr Leu Ala Cys Arg Asp Val Glu Lys Gly Glu Leu  
65 70 75 80  
Val Ala Lys Glu Ile Gln Thr Thr Thr Gly Asn Gln Gln Val Leu Val  
85 90 95  
Arg Lys Leu Asp Leu Ser Asp Thr Lys Ser Ile Arg Ala Phe Ala Lys  
100 105 110  
Gly Phe Leu Ala Glu Glu Lys His Leu His Val Leu Ile Asn Asn Ala  
115 120 125  
Gly Val Met Met Cys Pro Tyr Ser Lys Thr Ala Asp Gly Phe Glu Met  
130 135 140  
His Ile Gly Val Asn His Leu Gly His Phe Leu Leu Thr His Leu Leu  
145 150 155 160  
Leu Glu Lys Leu Lys Glu Ser Ala Pro Ser Arg Ile Val Asn Val Ser  
165 170 175  
Ser Leu Ala His His Leu Gly Arg Ile His Phe His Asn Leu Gln Gly  
180 185 190  
Glu Lys Phe Tyr Asn Ala Gly Leu Ala Tyr Cys His Ser Lys Leu Ala  
195 200 205  
Asn Ile Leu Phe Thr Gln Glu Leu Ala Arg Arg Leu Lys Gly Ser Gly  
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Val Thr Thr Tyr Ser Val His Pro Gly Thr Val Gln Ser Glu Leu Val  
225 230 235 240  
Arg His Ser Ser Phe Met Arg Trp Met Trp Trp Leu Phe Ser Phe Phe  
245 250 255  
Ile Lys Thr Pro Gln Gln Gly Ala Gln Thr Ser Leu His Cys Ala Leu  
260 265 270  
Thr Glu Gly Leu Glu Ile Leu Ser Gly Asn His Phe Ser Asp Cys His  
275 280 285  
Val Ala Trp Val Ser Ala Gln Ala Arg Asn Glu Thr Ile Ala Arg Arg  
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<213> Homo sapien

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111

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 <212> DNA  
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112

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<211> 282  
<212> DNA  
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<220>  
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gccctgcctc c

251

&lt;210&gt; 349

&lt;211&gt; 251

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 349

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&lt;210&gt; 350

&lt;211&gt; 908

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 350

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&lt;210&gt; 351

&lt;211&gt; 472

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 351

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&lt;210&gt; 352

&lt;211&gt; 251

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 352

114

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<210> 354  
 <211> 854  
 <212> DNA  
 <213> Homo sapien

<400> 354						
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gtgagtga	gatccccatt	ataggagcac	ttgggagaga	tcataataaa	gctgactctt	420
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tgaactggaa	aactaattca	aaagagagat	cgtgatatac	gtgtgggtga	tacaccttgg	600
caatatggaa	ggctctaatt	tgcccatatt	tgaataata	attcagcttt	ttgtaataca	660
aaataacaaa	gatttgagaa	tcattgtgtc	taatgtataa	aagaccagg	aaacataaat	720
atatcaactg	cataaatgta	aaatgcatgt	gacccaagaa	ggccccaag	tggcagacaa	780
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<210> 355  
 <211> 676  
 <212> DNA  
 <213> Homo sapien

<400> 355						
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atccacaagt	catacctgga	tgtcagcgaa	gagggcacgg	aggcagcagc	agccactggg	180
gacagcatcg	ctgtaaaaag	cctaccaatg	agagctcagt	tcaaggcgaa	ccacccttc	240
ctgttcttta	taaggcacac	tcataccaac	acgatcctat	tctgtggcaa	gcttgctctt	300
ccctaatacag	atgggggtga	gtaaggctca	gagttgcaga	tgagggtgcag	agacaatcct	360
gtgactttcc	cacggccaaa	aagctgttca	cacctcacgc	acctctgtgc	ctcagtttgc	420
tcactctgaa	aatagggtcta	ggatttcttc	caaccatttc	atgagttgtg	aagctaaggc	480
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115

ggtgtctcat ttgagtgtg tccagtgaca tgatcaagtc aatgagtaaa attttaaggg	600
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gcttaaagaa aaccag	676

<210> 356  
 <211> 574  
 <212> DNA  
 <213> Homo sapien

<400> 356	
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caagcttccc atttgtagat ctgagtcct atgagtatct gacacctgtt cctctcttca	180
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gagttctttt cttgggcaac agataaccag acaggactct aatcgtgctc ttattcaaca	360
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<210> 357  
 <211> 393  
 <212> DNA  
 <213> Homo sapien

<400> 357	
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aagccacaac caaracttga ttttatcaac aaaaaccctt aaatataaac ggsaaaaaag	180
atagatataa ttattccagt ttttttaaaa cttaaaarat attccattgc cgaattaara	240
araarataag tgttatatgg aaagaagggc attcaagcac actaaaraaa cctgaggkaa	300
gcataatctg taaaaaatta aactgtcctt tttggcattt taacaaattt gcaacgktct	360
tttttttctt tttctgtttt tttttttttt tac	393

<210> 358  
 <211> 630  
 <212> DNA  
 <213> Homo sapien

<400> 358	
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ttaatgttta taggaaaatg atgagtttat gacaaaggaa gtagatagtg ttttacaaga	120
gcatagagta ggaagctaa tccagcacag ggaggtcaca gagacatccc taaggaaagt	180
gagtttaaac tgagagaagc aagtgtctaa actgaaggat gtgttgaaga agaagggaga	240
gtagaacaat ttgggcagag ggaaccttat agaccctaag gtgggaaggt tcaagaagct	300
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tcaactgaagg gagtaatgtg acattacttt tcaactcagg atggccattc taactccagg	480
gggtagactg gactaggtaa gactggaggc aggtagacct cttctaaggc ctgcgatagt	540
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<210> 359  
 <211> 620  
 <212> DNA  
 <213> Homo sapien

116

&lt;400&gt; 359

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atggcattcc	ccaagggaaa	tagagagatt	cttctggatt	atgttcaata	tttatttcac	240
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aaagacaaca	tgatacctta	ggaagcaaca	ctaccctttc	aggcataaaa	tttgagaaa	360
tgcaacatta	tgcttcattg	ataatatgta	gaaagaaggt	ctgatgaaaa	tgacatcctt	420
aatgtaagat	aactttataa	gaattctggg	tcaaataaaa	ttctttgaag	aaaacatcca	480
aatgtcattg	acttatcaaa	tactatcttg	gcataatacc	tatgaaggca	aaactaaaca	540
aacaaaaagc	tcacaccaaa	caaaaccatc	aacttatttt	gtattctata	acatacgaga	600
ctgtaaaagt	gtgacagtgt					620

&lt;210&gt; 360

&lt;211&gt; 431

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 360

aaaaaaaaa	agccagaaca	acatgtgata	gataatatga	ttggctgcac	acttccagac	60
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tactcatcat	ttttggccag	cagttgtttg	atcaccaaac	atcatgccag	aatactcagc	180
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&lt;210&gt; 361

&lt;211&gt; 351

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 361

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ctgccactct	gtcctccagc	tctgacagct	cctcatctgt	ggctcctgtt	t	351

&lt;210&gt; 362

&lt;211&gt; 463

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 362

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tgtagatgag	ccggctgaag	atcttgcgca	tgccggcctt	cagggcgaag	ttcttgccgc	120
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cgtaaaggat	ttccgcgtcc	gtgtcgcagg	acagacgtat	atacttcctt	ttcttcccca	240
gtgtctcaaa	ctgaatatcc	ccaaaggcgt	cggtaggaaa	ttccttggtg	tgtttcttgt	300
agttccattt	ctcacttttg	ttgatctggg	tgcttccat	gtgtcggctc	tgggcatagc	360
cacacttgca	cacattctcc	ctgataagca	cgatgggtgtg	gacaggaagg	aaggatttca	420
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&lt;210&gt; 363

&lt;211&gt; 653

117

<212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(653)  
 <223> n = A,T,C or G

<400> 363

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atcttgagaa	tccttggtcc	agaattccat	ttacctctg	ggccagatac	caccagaatg	600
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<210> 364  
 <211> 401  
 <212> DNA  
 <213> Homo sapien

<400> 364

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aagtggatgc	gcggaaaatg	aaatcttctt	caatagccca	g		401

<210> 365  
 <211> 356  
 <212> DNA  
 <213> Homo sapien

<400> 365

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gactgtcacg	atgtgtatag	tacagtttga	caagcctggg	tccatacaga	ccgctggaga	300
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<210> 366  
 <211> 1851  
 <212> DNA  
 <213> Homo sapien

<400> 366

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tcacttcctt	taagcctttg	tgactcttcc	tctgatgtca	gctttaagtc	ttgttctgga	180
ttgctgtttt	cagaagagat	ttttaacatc	tgtttttctt	tgtagtcaga	aagtaactgg	240

118

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caaattacat gatgatgact agaaacagca tactctctgg ccgtctttcc agatcttgag 300
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cagcaagtat gagagcagtt cttccatatac tatccagcgc atttaaatc gcttttttct 420
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cttttcccca tttagtatta tgttggtgt gggctgtca taggtggttt ttattacttt 1800
aaggtatgtc ccttctatgc ctgttttgct gagggtttta attctcgtgc c 1851

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<210> 367  
 <211> 668  
 <212> DNA  
 <213> Homo sapien

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<400> 367
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gagtggtatt tccatactca tctggaatat ttggatcagt gccatgttcc agcaacatta 240
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gcagtcctat gagagtgaga agacttttta ggaaattgta gtgcactagc tacagccata 600
gcaatgattc atgtaactgc aaacactgaa tagcctgcta ttactctgcc ttcaaaaaaa 660
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<210> 368  
 <211> 1512  
 <212> DNA  
 <213> Homo sapien

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<400> 368
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119

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gcctgggtggg	gtaaaagccc	cagaaaggat	ctcatcgtca	tgctcaggga	cactgacgtg	720
aacaagaagg	acaagcaaaa	gaggactgct	ctacatctgg	cctctgccaa	tgggaattca	780
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agaagcatta	gaggttacag	tttttttttt	ttaaatgcac	ttctggtaaa	tacttttggt	1260
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taaaaaacag	taatagatac	gaggtgatgc	gcctgtcagt	ggcaagggtt	aagatatttc	1500
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&lt;210&gt; 369

&lt;211&gt; 1853

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 369

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tgggtcgtcc	gttgcttccc	ctgctgcagg	gagagcggca	agagcaacgt	gggcacttct	360
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 <213> Homo sapien

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 <213> Homo sapien

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&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 373

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&lt;211&gt; 2000

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 374

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 <212> PRT  
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124

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Val Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe Met Asp Pro Arg Tyr
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His Val His Gly Glu Asp Leu Asp Lys Leu His Arg Ala Ala Trp Trp
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Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met Leu Arg Asp Thr Asp
      130      135      140
Val Asn Lys Arg Asp Lys Gln Lys Arg Thr Ala Leu His Leu Ala Ser
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Ala Asn Gly Asn Ser Glu Val Val Lys Leu Val Leu Asp Arg Arg Cys
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Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr Ala Leu Thr Lys Ala
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Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr
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Ala Val Tyr Asn Glu Asp Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr
      225      230      235      240
Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly Leu Thr Pro Leu Leu
      245      250      255
Leu Gly Ile His Glu Gln Lys Gln Gln Val Val Lys Phe Leu Ile Lys
      260      265      270
Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr Gly Arg Thr Ala Leu
      275      280      285
Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile Val Ser Pro Leu Leu
      290      295      300
Glu Gln Asn Val Asp Val Ser Ser Gln Asp Leu Glu Arg Arg Pro Glu
      305      310      315      320
Ser Met Leu Phe Leu Val Ile Ile Met
      325

```

```

<210> 377
<211> 148
<212> PRT
<213> Homo sapien

```

```

<220>
<221> VARIANT
<222> (1)...(148)
<223> Xaa = Any Amino Acid

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```

<400> 377
Met Thr Xaa Pro Ser Trp Ser Pro Gly Thr Thr Ser Val Glu Lys Ile
  1      5      10      15
Trp Thr Ser Ser Thr Glu Leu Pro Trp Trp Gly Lys Val Pro Arg Lys
      20      25      30
Asp Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys Xaa Asp Lys
      35      40      45
Gln Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu

```

125

50 55 60  
 Val Val Lys Leu Xaa Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp  
 65 70 75 80  
 Asn Lys Lys Arg Thr Ala Leu Xaa Lys Ala Val Gln Cys Gln Glu Asp  
 85 90 95  
 Glu Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro  
 100 105 110  
 Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Xaa Tyr Asn Glu Asp  
 115 120 125  
 Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser  
 130 135 140  
 Lys Asn Lys Val  
 145

<210> 378  
 <211> 1719  
 <212> PRT  
 <213> Homo sapien

<400> 378  
 Met Val Val Glu Val Asp Ser Met Pro Ala Ala Ser Ser Val Lys Lys  
 1 5 10 15  
 Pro Phe Gly Leu Arg Ser Lys Met Gly Lys Trp Cys Cys Arg Cys Phe  
 20 25 30  
 Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp  
 35 40 45  
 His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp  
 50 55 60  
 Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val  
 65 70 75 80  
 Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn  
 85 90 95  
 Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys Cys Arg Gly Ser  
 100 105 110  
 Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe  
 115 120 125  
 Met Glu Pro Arg Tyr His Val Arg Gly Glu Asp Leu Asp Lys Leu His  
 130 135 140  
 Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met  
 145 150 155 160  
 Leu Arg Asp Thr Asp Val Asn Lys Lys Asp Lys Gln Lys Arg Thr Ala  
 165 170 175  
 Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu Val Val Lys Leu Leu  
 180 185 190  
 Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr  
 195 200 205  
 Ala Leu Ile Lys Ala Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met  
 210 215 220  
 Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn  
 225 230 235 240  
 Thr Thr Leu His Tyr Ala Ile Tyr Asn Glu Asp Lys Leu Met Ala Lys  
 245 250 255  
 Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly  
 260 265 270  
 Leu Thr Pro Leu Leu Leu Gly Val His Glu Gln Lys Gln Gln Val Val  
 275 280 285  
 Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr  
 290 295 300

Gly Arg Thr Ala Leu Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile  
 305 310 315 320  
 Val Ser Leu Leu Leu Glu Gln Asn Ile Asp Val Ser Ser Gln Asp Leu  
 325 330 335  
 Ser Gly Gln Thr Ala Arg Glu Tyr Ala Val Ser Ser His His Val  
 340 345 350  
 Ile Cys Gln Leu Leu Ser Asp Tyr Lys Glu Lys Gln Met Leu Lys Ile  
 355 360 365  
 Ser Ser Glu Asn Ser Asn Pro Glu Asn Val Ser Arg Thr Arg Asn Lys  
 370 375 380  
 Pro Arg Thr His Met Val Val Glu Val Asp Ser Met Pro Ala Ala Ser  
 385 390 395 400  
 Ser Val Lys Lys Pro Phe Gly Leu Arg Ser Lys Met Gly Lys Trp Cys  
 405 410 415  
 Cys Arg Cys Phe Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly  
 420 425 430  
 Thr Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys  
 435 440 445  
 Met Gly Lys Trp Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly  
 450 455 460  
 Lys Ser Asn Val Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys  
 465 470 475 480  
 Thr Leu Arg Asn Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys  
 485 490 495  
 Cys Arg Gly Ser Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp  
 500 505 510  
 Asp Ser Ala Phe Met Glu Pro Arg Tyr His Val Arg Gly Glu Asp Leu  
 515 520 525  
 Asp Lys Leu His Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp  
 530 535 540  
 Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys Lys Asp Lys Gln  
 545 550 555 560  
 Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu Val  
 565 570 575  
 Val Lys Leu Leu Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp Asn  
 580 585 590  
 Lys Lys Arg Thr Ala Leu Ile Lys Ala Val Gln Cys Gln Glu Asp Glu  
 595 600 605  
 Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro Asp  
 610 615 620  
 Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Ile Tyr Asn Glu Asp Lys  
 625 630 635 640  
 Leu Met Ala Lys Ala Leu Leu Tyr Gly Ala Asp Ile Glu Ser Lys  
 645 650 655  
 Asn Lys His Gly Leu Thr Pro Leu Leu Leu Gly Val His Glu Gln Lys  
 660 665 670  
 Gln Gln Val Val Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu Asn Ala  
 675 680 685  
 Leu Asp Arg Tyr Gly Arg Thr Ala Leu Ile Leu Ala Val Cys Cys Gly  
 690 695 700  
 Ser Ala Ser Ile Val Ser Leu Leu Leu Glu Gln Asn Ile Asp Val Ser  
 705 710 715 720  
 Ser Gln Asp Leu Ser Gly Gln Thr Ala Arg Glu Tyr Ala Val Ser Ser  
 725 730 735  
 His His His Val Ile Cys Gln Leu Leu Ser Asp Tyr Lys Glu Lys Gln  
 740 745 750  
 Met Leu Lys Ile Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys  
 755 760 765

Leu Thr Ser Glu Glu Glu Ser Gln Arg Phe Lys Gly Ser Glu Asn Ser  
 770 775 780  
 Gln Pro Glu Lys Met Ser Gln Glu Pro Glu Ile Asn Lys Asp Gly Asp  
 785 790 795 800  
 Arg Glu Val Glu Glu Met Lys Lys His Glu Ser Asn Asn Val Gly  
 805 810 815  
 Leu Leu Glu Asn Leu Thr Asn Gly Val Thr Ala Gly Asn Gly Asp Asn  
 820 825 830  
 Gly Leu Ile Pro Gln Arg Lys Ser Arg Thr Pro Glu Asn Gln Gln Phe  
 835 840 845  
 Pro Asp Asn Glu Ser Glu Glu Tyr His Arg Ile Cys Glu Leu Val Ser  
 850 855 860  
 Asp Tyr Lys Glu Lys Gln Met Pro Lys Tyr Ser Ser Glu Asn Ser Asn  
 865 870 875 880  
 Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu Glu Ser Gln Arg Leu  
 885 890 895  
 Glu Gly Ser Glu Asn Gly Gln Pro Glu Leu Glu Asn Phe Met Ala Ile  
 900 905 910  
 Glu Glu Met Lys Lys His Gly Ser Thr His Val Gly Phe Pro Glu Asn  
 915 920 925  
 Leu Thr Asn Gly Ala Thr Ala Gly Asn Gly Asp Asp Gly Leu Ile Pro  
 930 935 940  
 Pro Arg Lys Ser Arg Thr Pro Glu Ser Gln Gln Phe Pro Asp Thr Glu  
 945 950 955 960  
 Asn Glu Glu Tyr His Ser Asp Glu Gln Asn Asp Thr Gln Lys Gln Phe  
 965 970 975  
 Cys Glu Glu Gln Asn Thr Gly Ile Leu His Asp Glu Ile Leu Ile His  
 980 985 990  
 Glu Glu Lys Gln Ile Glu Val Val Glu Lys Met Asn Ser Glu Leu Ser  
 995 1000 1005  
 Leu Ser Cys Lys Lys Glu Lys Asp Ile Leu His Glu Asn Ser Thr Leu  
 1010 1015 1020  
 Arg Glu Glu Ile Ala Met Leu Arg Leu Glu Leu Asp Thr Met Lys His  
 1025 1030 1035 1040  
 Gln Ser Gln Leu Pro Arg Thr His Met Val Val Glu Val Asp Ser Met  
 1045 1050 1055  
 Pro Ala Ala Ser Ser Val Lys Lys Pro Phe Gly Leu Arg Ser Lys Met  
 1060 1065 1070  
 Gly Lys Trp Cys Cys Arg Cys Phe Pro Cys Cys Arg Glu Ser Gly Lys  
 1075 1080 1085  
 Ser Asn Val Gly Thr Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr  
 1090 1095 1100  
 Leu Arg Ser Lys Met Gly Lys Trp Cys Arg His Cys Phe Pro Cys Cys  
 1105 1110 1115 1120  
 Arg Gly Ser Gly Lys Ser Asn Val Gly Ala Ser Gly Asp His Asp Asp  
 1125 1130 1135  
 Ser Ala Met Lys Thr Leu Arg Asn Lys Met Gly Lys Trp Cys Cys His  
 1140 1145 1150  
 Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Lys Val Gly Ala Trp  
 1155 1160 1165  
 Gly Asp Tyr Asp Asp Ser Ala Phe Met Glu Pro Arg Tyr His Val Arg  
 1170 1175 1180  
 Gly Glu Asp Leu Asp Lys Leu His Arg Ala Ala Trp Trp Gly Lys Val  
 1185 1190 1195 1200  
 Pro Arg Lys Asp Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys  
 1205 1210 1215  
 Lys Asp Lys Gln Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly  
 1220 1225 1230



Asn Ser Glu Val Val Lys Leu Leu Leu Asp Arg Arg Cys Gln Leu Asn  
 1235 1240 1245  
 Val Leu Asp Asn Lys Lys Arg Thr Ala Leu Ile Lys Ala Val Gln Cys  
 1250 1255 1260  
 Gln Glu Asp Glu Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro  
 1265 1270 1275 1280  
 Asn Ile Pro Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Ile Tyr  
 1285 1290 1295  
 Asn Glu Asp Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr Gly Ala Asp  
 1300 1305 1310  
 Ile Glu Ser Lys Asn Lys His Gly Leu Thr Pro Leu Leu Leu Gly Val  
 1315 1320 1325  
 His Glu Gln Lys Gln Gln Val Val Lys Phe Leu Ile Lys Lys Lys Ala  
 1330 1335 1340  
 Asn Leu Asn Ala Leu Asp Arg Tyr Gly Arg Thr Ala Leu Ile Leu Ala  
 1345 1350 1355 1360  
 Val Cys Cys Gly Ser Ala Ser Ile Val Ser Leu Leu Leu Glu Gln Asn  
 1365 1370 1375  
 Ile Asp Val Ser Ser Gln Asp Leu Ser Gly Gln Thr Ala Arg Glu Tyr  
 1380 1385 1390  
 Ala Val Ser Ser His His His Val Ile Cys Gln Leu Leu Ser Asp Tyr  
 1395 1400 1405  
 Lys Glu Lys Gln Met Leu Lys Ile Ser Ser Glu Asn Ser Asn Pro Glu  
 1410 1415 1420  
 Gln Asp Leu Lys Leu Thr Ser Glu Glu Glu Ser Gln Arg Phe Lys Gly  
 1425 1430 1435 1440  
 Ser Glu Asn Ser Gln Pro Glu Lys Met Ser Gln Glu Pro Glu Ile Asn  
 1445 1450 1455  
 Lys Asp Gly Asp Arg Glu Val Glu Glu Glu Met Lys Lys His Glu Ser  
 1460 1465 1470  
 Asn Asn Val Gly Leu Leu Glu Asn Leu Thr Asn Gly Val Thr Ala Gly  
 1475 1480 1485  
 Asn Gly Asp Asn Gly Leu Ile Pro Gln Arg Lys Ser Arg Thr Pro Glu  
 1490 1495 1500  
 Asn Gln Gln Phe Pro Asp Asn Glu Ser Glu Glu Tyr His Arg Ile Cys  
 1505 1510 1515 1520  
 Glu Leu Val Ser Asp Tyr Lys Glu Lys Gln Met Pro Lys Tyr Ser Ser  
 1525 1530 1535  
 Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu Glu Glu  
 1540 1545 1550  
 Ser Gln Arg Leu Glu Gly Ser Glu Asn Gly Gln Pro Glu Lys Arg Ser  
 1555 1560 1565  
 Gln Glu Pro Glu Ile Asn Lys Asp Gly Asp Arg Glu Leu Glu Asn Phe  
 1570 1575 1580  
 Met Ala Ile Glu Glu Met Lys Lys His Gly Ser Thr His Val Gly Phe  
 1585 1590 1595 1600  
 Pro Glu Asn Leu Thr Asn Gly Ala Thr Ala Gly Asn Gly Asp Asp Gly  
 1605 1610 1615  
 Leu Ile Pro Pro Arg Lys Ser Arg Thr Pro Glu Ser Gln Gln Phe Pro  
 1620 1625 1630  
 Asp Thr Glu Asn Glu Glu Tyr His Ser Asp Glu Gln Asn Asp Thr Gln  
 1635 1640 1645  
 Lys Gln Phe Cys Glu Glu Gln Asn Thr Gly Ile Leu His Asp Glu Ile  
 1650 1655 1660  
 Leu Ile His Glu Glu Lys Gln Ile Glu Val Val Glu Lys Met Asn Ser  
 1665 1670 1675 1680  
 Glu Leu Ser Leu Ser Cys Lys Lys Glu Lys Asp Ile Leu His Glu Asn  
 1685 1690 1695

Ser Thr Leu Arg Glu Glu Ile Ala Met Leu Arg Leu Glu Leu Asp Thr  
 1700 1705 1710  
 Met Lys His Gln Ser Gln Leu  
 1715

<210> 379  
 <211> 656  
 <212> PRT  
 <213> Homo sapien

<400> 379  
 Met Val Val Glu Val Asp Ser Met Pro Ala Ala Ser Ser Val Lys Lys  
 1 5 10 15  
 Pro Phe Gly Leu Arg Ser Lys Met Gly Lys Trp Cys Cys Arg Cys Phe  
 20 25 30  
 Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp  
 35 40 45  
 His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp  
 50 55 60  
 Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val  
 65 70 75 80  
 Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn  
 85 90 95  
 Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys Cys Arg Gly Ser  
 100 105 110  
 Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe  
 115 120 125  
 Met Glu Pro Arg Tyr His Val Arg Gly Glu Asp Leu Asp Lys Leu His  
 130 135 140  
 Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met  
 145 150 155 160  
 Leu Arg Asp Thr Asp Val Asn Lys Lys Asp Lys Gln Lys Arg Thr Ala  
 165 170 175  
 Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu Val Val Lys Leu Leu  
 180 185 190  
 Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr  
 195 200 205  
 Ala Leu Ile Lys Ala Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met  
 210 215 220  
 Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn  
 225 230 235 240  
 Thr Thr Leu His Tyr Ala Ile Tyr Asn Glu Asp Lys Leu Met Ala Lys  
 245 250 255  
 Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly  
 260 265 270  
 Leu Thr Pro Leu Leu Leu Gly Val His Glu Gln Lys Gln Gln Val Val  
 275 280 285  
 Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr  
 290 295 300  
 Gly Arg Thr Ala Leu Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile  
 305 310 315 320  
 Val Ser Leu Leu Leu Glu Gln Asn Ile Asp Val Ser Ser Gln Asp Leu  
 325 330 335  
 Ser Gly Gln Thr Ala Arg Glu Tyr Ala Val Ser Ser His His His Val  
 340 345 350  
 Ile Cys Gln Leu Leu Ser Asp Tyr Lys Glu Lys Gln Met Leu Lys Ile  
 355 360 365  
 Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu

130

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      370              375              380
Glu Glu Ser Gln Arg Phe Lys Gly Ser Glu Asn Ser Gln Pro Glu Lys
385              390              395              400
Met Ser Gln Glu Pro Glu Ile Asn Lys Asp Gly Asp Arg Glu Val Glu
      405              410              415
Glu Glu Met Lys Lys His Glu Ser Asn Asn Val Gly Leu Leu Glu Asn
      420              425              430
Leu Thr Asn Gly Val Thr Ala Gly Asn Gly Asp Asn Gly Leu Ile Pro
      435              440              445
Gln Arg Lys Ser Arg Thr Pro Glu Asn Gln Gln Phe Pro Asp Asn Glu
      450              455              460
Ser Glu Glu Tyr His Arg Ile Cys Glu Leu Val Ser Asp Tyr Lys Glu
465              470              475              480
Lys Gln Met Pro Lys Tyr Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp
      485              490              495
Leu Lys Leu Thr Ser Glu Glu Glu Ser Gln Arg Leu Glu Gly Ser Glu
      500              505              510
Asn Gly Gln Pro Glu Leu Glu Asn Phe Met Ala Ile Glu Glu Met Lys
      515              520              525
Lys His Gly Ser Thr His Val Gly Phe Pro Glu Asn Leu Thr Asn Gly
      530              535              540
Ala Thr Ala Gly Asn Gly Asp Asp Gly Leu Ile Pro Pro Arg Lys Ser
545              550              555              560
Arg Thr Pro Glu Ser Gln Gln Phe Pro Asp Thr Glu Asn Glu Glu Tyr
      565              570              575
His Ser Asp Glu Gln Asn Asp Thr Gln Lys Gln Phe Cys Glu Glu Gln
      580              585              590
Asn Thr Gly Ile Leu His Asp Glu Ile Leu Ile His Glu Glu Lys Gln
      595              600              605
Ile Glu Val Val Glu Lys Met Asn Ser Glu Leu Ser Leu Ser Cys Lys
      610              615              620
Lys Glu Lys Asp Ile Leu His Glu Asn Ser Thr Leu Arg Glu Glu Ile
625              630              635              640
Ala Met Leu Arg Leu Glu Leu Asp Thr Met Lys His Gln Ser Gln Leu
      645              650              655

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<210> 380
<211> 671
<212> PRT
<213> Homo sapien

```

```

<400> 380
Met Val Val Glu Val Asp Ser Met Pro Ala Ala Ser Ser Val Lys Lys
 1              5              10              15
Pro Phe Gly Leu Arg Ser Lys Met Gly Lys Trp Cys Cys Arg Cys Phe
      20              25              30
Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp
      35              40              45
His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp
      50              55              60
Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val
65              70              75              80
Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn
      85              90              95
Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys Cys Arg Gly Ser
      100              105              110
Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe
      115              120              125

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Met	Glu	Pro	Arg	Tyr	His	Val	Arg	Gly	Glu	Asp	Leu	Asp	Lys	Leu	His
130						135					140				
Arg	Ala	Ala	Trp	Trp	Gly	Lys	Val	Pro	Arg	Lys	Asp	Leu	Ile	Val	Met
145					150					155					160
Leu	Arg	Asp	Thr	Asp	Val	Asn	Lys	Lys	Asp	Lys	Gln	Lys	Arg	Thr	Ala
				165					170					175	
Leu	His	Leu	Ala	Ser	Ala	Asn	Gly	Asn	Ser	Glu	Val	Val	Lys	Leu	Leu
			180					185					190		
Leu	Asp	Arg	Arg	Cys	Gln	Leu	Asn	Val	Leu	Asp	Asn	Lys	Lys	Arg	Thr
		195					200					205			
Ala	Leu	Ile	Lys	Ala	Val	Gln	Cys	Gln	Glu	Asp	Glu	Cys	Ala	Leu	Met
210						215					220				
Leu	Leu	Glu	His	Gly	Thr	Asp	Pro	Asn	Ile	Pro	Asp	Glu	Tyr	Gly	Asn
225					230					235					240
Thr	Thr	Leu	His	Tyr	Ala	Ile	Tyr	Asn	Glu	Asp	Lys	Leu	Met	Ala	Lys
				245					250					255	
Ala	Leu	Leu	Leu	Tyr	Gly	Ala	Asp	Ile	Glu	Ser	Lys	Asn	Lys	His	Gly
			260					265					270		
Leu	Thr	Pro	Leu	Leu	Leu	Gly	Val	His	Glu	Gln	Lys	Gln	Gln	Val	Val
		275					280					285			
Lys	Phe	Leu	Ile	Lys	Lys	Lys	Ala	Asn	Leu	Asn	Ala	Leu	Asp	Arg	Tyr
		290				295					300				
Gly	Arg	Thr	Ala	Leu	Ile	Leu	Ala	Val	Cys	Cys	Gly	Ser	Ala	Ser	Ile
305					310					315					320
Val	Ser	Leu	Leu	Leu	Glu	Gln	Asn	Ile	Asp	Val	Ser	Ser	Gln	Asp	Leu
				325					330					335	
Ser	Gly	Gln	Thr	Ala	Arg	Glu	Tyr	Ala	Val	Ser	Ser	His	His	His	Val
			340					345					350		
Ile	Cys	Gln	Leu	Leu	Ser	Asp	Tyr	Lys	Glu	Lys	Gln	Met	Leu	Lys	Ile
		355					360					365			
Ser	Ser	Glu	Asn	Ser	Asn	Pro	Glu	Gln	Asp	Leu	Lys	Leu	Thr	Ser	Glu
		370				375					380				
Glu	Glu	Ser	Gln	Arg	Phe	Lys	Gly	Ser	Glu	Asn	Ser	Gln	Pro	Glu	Lys
385					390					395					400
Met	Ser	Gln	Glu	Pro	Glu	Ile	Asn	Lys	Asp	Gly	Asp	Arg	Glu	Val	Glu
				405					410					415	
Glu	Glu	Met	Lys	Lys	His	Glu	Ser	Asn	Asn	Val	Gly	Leu	Leu	Glu	Asn
			420					425					430		
Leu	Thr	Asn	Gly	Val	Thr	Ala	Gly	Asn	Gly	Asp	Asn	Gly	Leu	Ile	Pro
		435					440					445			
Gln	Arg	Lys	Ser	Arg	Thr	Pro	Glu	Asn	Gln	Gln	Phe	Pro	Asp	Asn	Glu
		450				455					460				
Ser	Glu	Glu	Tyr	His	Arg	Ile	Cys	Glu	Leu	Val	Ser	Asp	Tyr	Lys	Glu
465					470					475					480
Lys	Gln	Met	Pro	Lys	Tyr	Ser	Ser	Glu	Asn	Ser	Asn	Pro	Glu	Gln	Asp
				485					490					495	
Leu	Lys	Leu	Thr	Ser	Glu	Glu	Glu	Ser	Gln	Arg	Leu	Glu	Gly	Ser	Glu
			500					505					510		
Asn	Gly	Gln	Pro	Glu	Lys	Arg	Ser	Gln	Glu	Pro	Glu	Ile	Asn	Lys	Asp
		515					520					525			
Gly	Asp	Arg	Glu	Leu	Glu	Asn	Phe	Met	Ala	Ile	Glu	Glu	Met	Lys	Lys
530						535					540				
His	Gly	Ser	Thr	His	Val	Gly	Phe	Pro	Glu	Asn	Leu	Thr	Asn	Gly	Ala
545					550					555					560
Thr	Ala	Gly	Asn	Gly	Asp	Asp	Gly	Leu	Ile	Pro	Pro	Arg	Lys	Ser	Arg
				565					570					575	
Thr	Pro	Glu	Ser	Gln	Gln	Phe	Pro	Asp	Thr	Glu	Asn	Glu	Glu	Tyr	His
			580					585						590	

132

Ser Asp Glu Gln Asn Asp Thr Gln Lys Gln Phe Cys Glu Glu Gln Asn  
 595 600 605  
 Thr Gly Ile Leu His Asp Glu Ile Leu Ile His Glu Glu Lys Gln Ile  
 610 615 620  
 Glu Val Val Glu Lys Met Asn Ser Glu Leu Ser Leu Ser Cys Lys Lys  
 625 630 635 640  
 Glu Lys Asp Ile Leu His Glu Asn Ser Thr Leu Arg Glu Glu Ile Ala  
 645 650 655  
 Met Leu Arg Leu Glu Leu Asp Thr Met Lys His Gln Ser Gln Leu  
 660 665 670

<210> 381  
 <211> 251  
 <212> DNA  
 <213> Homo sapien

<400> 381  
 ggagaagcgt ctgctggggc aggaaggggt ttccctgccc tctcacctgt cctcaccaa 60  
 ggtaacatgc ttcccctaag ggtatcccaa cccaggggcc tcaccatgac ctctgagggg 120  
 ccaatatccc aggagaagca ttggggaggt gggggcaggt gaaggaccca ggactcacac 180  
 atcctggggc tccaaggcag aggagagggt cctcaagaag gtcaggagga aaatccgtaa 240  
 caagcagtca g 251

<210> 382  
 <211> 3279  
 <212> DNA  
 <213> Homo sapiens

<400> 382  
 cttcctgcag ccccatgct ggtgaggggc acggggcagga acagtggacc caacatgaa 60  
 atgctggagg gtgtcaggaa gtgatcgggc tctggggcag ggaggagggg tggggagtgt 120  
 cactgggagg ggacatcctg cagaaggtag gagtgagcaa acaccgctg caggggaggg 180  
 gagagccctg cggcacctgg gggagcagag ggagcagcac ctggccaggc ctgggaggag 240  
 gggcctggag ggcgtgagga ggagcgaggg ggctgcatgg ctggagttag ggtcagggg 300  
 cagggcgcgga gatggcctca cacagggaag agaggggccc tctgcaggg cctcacctgg 360  
 gccacaggag gacactgctt ttctctgag gagtcaggag ctgtggatgg tggctggacag 420  
 aagaaggaca gggcctggct caggtgtcca gaggtgtcgg ctggcttccc ttggggatca 480  
 gactgcaggg agggagggcg gcagggttgt ggggggagtg acgatgagga tgacctgggg 540  
 gtggctccag gccttgcccc tgcctggggc ctaccacagc ctccctcaca gtctcctggc 600  
 cctcagtcct tcccctccac tccatcctcc atctggcctc agtgggtcat tctgatcact 660  
 gaactgacca taccagccc tgcccacggc cctccatggc tcccaatgc cctggagagg 720  
 ggacatctag tcagagagta gtctgaaga ggtggcctct gcgatgtgcc tgtgggggca 780  
 gcatcctgca gatggtcccg gccctcatcc tgctgacctg tctgcaggga ctgtcctcct 840  
 ggacctggcc ccttgtgcag gagctggacc ctgaagtccc ctcccatag gccaaactg 900  
 gagccttgtt ccctctgttg gactccctgc ccatattctt gtgggagtggt gttctggaga 960  
 catttctgtc tgttctctgag agctgggaat tgctctcagt catctgcctg cgcggttctg 1020  
 agagatggag ttgcctaggc agttattggg gccaatcttt ctactgtgt ctctcctcct 1080  
 ttacccttag ggtgattctg ggggtccact tgtctgtaat ggtgtgcttc aaggatcac 1140  
 atcatggggc cctgagccat gtgccctgcc tgaaaagcct gctgtgtaca ccaaggtggt 1200  
 gcattaccgg aagtggatca aggacaccat cgcagccaac ccctgagtgcc cctgttccca 1260  
 cccctacctc tagtaaatat aagtccacct cacgttcttg catcacttg cctttctgga 1320  
 tgcctggacac ctgaagcttg gaactcacct ggccgaagct cgagcctcct gactcctact 1380  
 gacctgtgct ttctgtgttg gagtccaggg ctgctaggaa aaggaatggg cagacacagg 1440  
 tgtatgcaa tgtttctgaa atgggtataa tttcgtctc tcttcggaa cactggctgt 1500  
 ctctgaagac ttctcgctca gtttcagtga ggacacacac aaagacgtgg gtgacctagt 1560  
 tgtttgtggg gtgcagagat gggaggggtg gggcccaccc tggaagagtg gacagtga 1620  
 caaggtggac actctctaca gatcactgag gataagctgg agccacaatg catgaggcac 1680  
 acacacagca aggttgacgc tgtaaacata gccacgctg tctggggggc actgggaagc 1740

```

ctagataagg ccgtgagcag aaagaagggg aggatcctcc tatgttgttg aaggaggggac 1800
taggggggaga aactgaaagc tgattaatta caggaggttt gttcagggtcc cccaaaccac 1860
cgctcagattt gatgatttcc tagcaggact tacagaaata aagagctatc atgctgtggt 1920
ttattatggt ttgttacatt gataggatac atactgaaat cagcaaaca aacagatgta 1980
tagattagag tgtggagaaa acagaggaaa acttgagtt acgaagactg gcaacttggc 2040
tttactaagt tttcagactg gcaggaagtc aaacctatta ggctgaggac cttgtggagt 2100
gtagctgatac cagctgatag aggaactagc caggtggggg cctttccctt tggatggggg 2160
gcatatccga cagtatttct ctccaagtgg agacttacgg acagcatata attctccctg 2220
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gtgtccaggg tttttactgg gggctctgtg gacgagtatg gactacttga ataattgacc 2340
tgaagtcctc agacctgagg ttccctagag ttcaaacaga tacagcatgg tccagagtcc 2400
cagatgtaca aaaacaggga ttcatcaca atcccatctt tagcatgaag ggtctggcat 2460
ggcccaaggc cccaagtata tcaaggcact tgggcagAAC atgccaagga atcaaatgtc 2520
atctcccagg agttattcaa gggtagagccc tttacttggg atgtacaggg tttgagcagt 2580
gcagggctgc tgagtcaacc ttttattgta caggggatga gggaaagggg gaggatgagg 2640
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atcattgttt tatttgcctt cttttcacac cattggtgag ggagggatta ccaccctggg 2820
gttatgaaga tggttgaaca cccacacatc agcaccggag atatgagatc aacagtttct 2880
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ggggatgcgc tcgggatttg tgtgaagaag caaggactgt tagaggcagg ctttatagta 3000
acaagacggt ggggcaact ctgatttccg tgggggaatg tcatggtctt gctttactaa 3060
gttttgagac tggcaggtag tgaaactcat taggctgaga accttgtgga atgcagctga 3120
cccagctgat agaggaagta gccaggtggg agcctttccc agtggtgtg ggacatatct 3180
ggcaagattt tgtggcactc ctggttacag atactggggc agcaaataaa actgaatctt 3240
gttttcagac cttaaaaaaa aaaaaaaaaa aaaagtttt 3279

```

&lt;210&gt; 383

&lt;211&gt; 154

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 383

```

Met Ala Gly Val Arg Asp Gln Gly Gln Gly Ala Arg Trp Pro His Thr
      5              10              15
Gly Lys Arg Gly Pro Leu Leu Gln Gly Leu Thr Trp Ala Thr Gly Gly
      20              25              30
His Cys Phe Ser Ser Glu Glu Ser Gly Ala Val Asp Gly Ala Gly Gln
      35              40              45
Lys Lys Asp Arg Ala Trp Leu Arg Cys Pro Glu Ala Val Ala Gly Phe
      50              55              60
Pro Leu Gly Ser Asp Cys Arg Glu Gly Gly Arg Gln Gly Cys Gly Gly
      65              70              75
Ser Asp Asp Glu Asp Asp Leu Gly Val Ala Pro Gly Leu Ala Pro Ala
      85              90              95
Trp Ala Leu Thr Gln Pro Pro Ser Gln Ser Pro Gly Pro Gln Ser Leu
      100             105             110
Pro Ser Thr Pro Ser Ser Ile Trp Pro Gln Trp Val Ile Leu Ile Thr
      115             120             125
Glu Leu Thr Ile Pro Ser Pro Ala His Gly Pro Pro Trp Leu Pro Asn
      130             135             140
Ala Leu Glu Arg Gly His Leu Val Arg Glu
      145             150

```

&lt;210&gt; 384

&lt;211&gt; 557

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 384

```

ggatcctcta gagcgccgc ctactactac taaattcgcg gccgcgtcga cgaagaagag 60
aaagatgtgt tttgttttg actctctgtg gtcccttcca atgctgtggg tttccaacca 120
ggggaagggt cccttttgca ttgccaagt ccataaccat gagcactact ctaccatggt 180
tctgcctcct ggccaagcag gctggtttgc aagaatgaaa tgaatgattc tacagctagg 240
acttaacctt gaaatggaaa gtcttgcaat cccatttgca ggatccgtct gtgcacatgc 300
ctctgtagag agcagcattc ccagggacct tggaaacagt tggcactgta aggtgcttgc 360
tccccaagac acatcctaaa aggtgttgta atggtgaaaa cgtcttcctt ctttattgcc 420
ccttccttatt tatgtgaaca actgtttgtc tttttttgta tcttttttaa actgtaaagt 480
tcaattgtga aaatgaatat catgcaaata aattatgcga ttttttttcc aaagtaaaaa 540
aaaaaaaaa aaaaaaa 557

```

&lt;210&gt; 385

&lt;211&gt; 337

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 385

```

ttcccagggt atgtgcgagg gaagacacat ttactatcct tgatggggct gattccttta 60
gtttctctag cagcagatgg gttaggagga agtgacccaa gtggttgact cctatgtgca 120
tctcaaagcc atctgctgtc ttcgagtacg gacacatcat cactcctgca ttgttgatca 180
aaacgtggag gtgcttttcc tcagctaaga agcccttagc aaaagctcga atagacttag 240
tatcagacag gtcagtttc cgcaccaaca cctgctggtt ccctgtcgtg gtctggatct 300
ctttggccac caattccccc tttccacat cccggca 337

```

&lt;210&gt; 386

&lt;211&gt; 300

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 386

```

gggcccgtca ccggcccagg cccgcctcg cgagtcctcc tccccgggtg cctgcccgca 60
gcccgtctcg cccagagggt gggcgcgagg ctgcctctac cggctggcgg ctgtaactca 120
gcgaccttgg cccgaaggct ctagcaagga cccaccgacc ccagccgagg cggcgggcggc 180
gcggactttg cccggtgtgt ggggcggagc ggactgcgtg tccgcggacg ggcagcgaag 240
atgttagcct tcgtgccag gaccgtggac cgatcccagg gctgtggtgt aacctcagcc 300

```

&lt;210&gt; 387

&lt;211&gt; 537

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 387

```

gggcccagtc gggcaccaag ggactctttg caggcttcct tcctcggatc atcaaggctg 60
ccccctctcg tgccatcatg atcagcacct atgagttcgg caaaagcttc ttccagaggc 120
tgaaccagga ccggcttctg ggcggctgaa aggggcaagg aggcaaggac cccgtctctc 180
ccacggatgg ggagagggca ggaggagacc cagccaagt ccttttcttc agcactgagg 240
gagggggctt gtttcccttc cctccggcg acaagctcca gggcagggct gtccctctgg 300
gcggcccagc acttctcag acacaacttc ttctgctgc tccagtcgtg gggatcatca 360
cttaccaccc cccaagttc aagaccaa atctccagctg ccccttcgt gtttccctgt 420
gtttgctgta gctgggcatg tctccaggaa ccaagaagcc ctcagcctgg tgtagtctcc 480
ctgacccttg ttaattcctt aagtctaaag atgatgaact tcaaaaaaa aaaaaaa 537

```

&lt;210&gt; 388

&lt;211&gt; 520

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 388

```
aggataattt ttaaaccaat caaatgaaaa aaacaaacaa acaaaaaagg aaatgtcatg 60
tgagggttaaa ccagtttgca ttcccctaata gtggaaaaag taagaggact actcagcact 120
gtttgaagat tgccctcttct acagcttctg agaatttgtt tatttcactt gccaaagtga 180
ggacccccctc cccaacatgc ccagcccccac cctaagcat ggtcccttgt caccaggcaa 240
ccaggaaact gctacttgtg gacctcacca gagaccagga ggggttggtt agctcacagg 300
acttccccca cccagaaga ttagcatccc atactagact cataactcaac tcaactaggc 360
tcatactcaa ttgatgggta ttagacaatt ccatttcttt ctgggttatta taaacagaaa 420
atctttcctc ttctcattac cagtaaaggc tcttggtatc tttctgttgg aatgatttct 480
atgaacttgt cttattttaa tgggtgggtt ttttctggt 520
```

&lt;210&gt; 389

&lt;211&gt; 365

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 389

```
cgttgcccca gtttgacaga aggaaaggcg gagcttattc aaagtctaga gggagtggag 60
gagttaaggc tggatttcag atctgcctgg ttccagccgc agtgtgccct ctgctcccc 120
aacgactttc caaataatct caccagcgcc ttccagctca ggcgtcctag aagcgtcttg 180
aagcctatgg ccagctgtct ttgtgttccc tctcaccgcg ctgtcctcac agctgagact 240
cccaggaaac cttcagacta ccttctctctg ccttcagcaa ggggcgttgc ccacattctc 300
tgagggtcag tggaagaacc tagactccca ttgctagagg tagaaagggg aagggtgctg 360
gggag 365
```

&lt;210&gt; 390

&lt;211&gt; 221

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(221)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 390

```
tgctcttcca tcttggtccc gacttctctg tcaggaaagt ggggatggac cccatctgca 60
tacacggntt ctcatgggtg tggaacatct ctgcttgccg ttccaggaag gcctctggct 120
gctctangag tctgancnga ntcgttgccc cantntgaca naaggaaagg cggagcttat 180
tcaaagtcta gaggagtggt aggagttaag gctggatttc a 221
```

&lt;210&gt; 391

&lt;211&gt; 325

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(325)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 391

```
tggagcaggt cccaggcct ccctagagcc tggggccgac tctgtgncga tgcangcttt 60
ctctcgcgcc cagcctggag ctgctcctgg catctaccaa caatcagncg aggcgagcag 120
tagccagggc actgctgcca acagccagtc cnnataccat catgtnaccc ggtgngctct 180
naantngat ntccanagcc ctaccatcn tagttctgct ctcccaccgg ntaccagccc 240
cactgcccag gaatcctaca gccagtaccc tgtcccgacg tctctaccta ccagtacgat 300
```



136

gagacctccg gctactacta tgacc

325

&lt;210&gt; 392

&lt;211&gt; 277

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(277)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 392

```
atattgttta actccttcct ttatatcttt taacattttc atggngaaag gttcacatct 60
agtctcactt nggcnagn gn ctcctacttg agtctcttcc ccggcctgnn ccagtngnaa 120
antaccanga accgncatgn cttanaaen ncctggtttn tgggttnntc aatgactgca 180
tgacgtgcac caccctgtcc actacgtgat gctgtaggat taaagtctca cagtgggcgg 240
ctgaggatac agcgccgcgt cctgtgttgc tggggaa 277
```

&lt;210&gt; 393

&lt;211&gt; 566

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 393

```
actagtccag tgtggtggaa ttccggcccg cgtcgacgga caggtcagct gtctggctca 60
gtgatctaca ttctgaagtt gtctgaaaat gtcttcatga tttaaattcag cctaaacggt 120
ttgccgggaa cactgcagag acaatgctgt gagtttccaa ccttagccca tctgcccggca 180
gagaaggctc agtttgtcca tcagcattat catgatatac ggactgggta cttgggtaag 240
gaggggtcta ggagatctgt cccttttaga gacaccttac ttataatgaa gtatttggga 300
gggtgggttt caaaagtaga aatgtcctgt attccgatga tcatcctgta aacattttat 360
catttattaa tcatccctgc ctgtgtctat tattatattc atatctctac gctggaaact 420
ttctgcctca atgtttactg tgcctttgtt ttgctagtgt tgtgtgtgtg aaaaaaaaaa 480
cattctctgc ctgagtttta attttgtcc aaagtatttt taatctatac aattaaaagc 540
ttttgcctat caaaaaaaaa aaaaaa 566
```

&lt;210&gt; 394

&lt;211&gt; 384

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(384)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 394

```
gaacatacat gtcccggcac ctgagctgca gtctgacatc atcgccatca cgggcctcgc 60
tgcaaattng gaccgggcca aggctggact gctggagcgt gtgaaggagc tacaggccna 120
gcaggaggac cgggctttta ggagttttta gctgagtgtc actgtagacc ccaaatacca 180
tccaagatt atcgggagaa agggggcagt aattacccaa atccgggttg agcatgacgt 240
gaacatccag tttcctgata aggacgatgg gaaccagccc caggaccaa ttaccatcac 300
agggtacgaa aagaacacag aagctgccag ggatgctata ctgagaattg tgggtgaact 360
tgagcagatg gtttctgagg acgt 384
```

&lt;210&gt; 395

&lt;211&gt; 399

&lt;212&gt; DNA

<213> Homo sapiens

<400> 395

```
ggcaaaactg tgtgacctca ataagacctc gcagatocaa ggtcaagtat cagaagtgac 60
tctgaccttg gactccaaga cctacatcaa cagcctggct atattagatg atgagccagt 120
tatcagaggt ttcacatttg cggaattgt ggagtctaag gaaatcatgg cctctgaagt 180
attcacgtct ttccagtacc ctgagttctc tatagagttg cctaacacag gcagaattgg 240
ccagctactt gtctgcaatt gtatcttcaa gaatacctg gccatccctt tgactgacgt 300
caagttctct ttggaagcc tgggcatctc ctactacag acctctgacc atgggacggt 360
gcagcctggt gagaccatcc aatcccaaat aaaatgcac 399
```

<210> 396

<211> 403

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(403)

<223> n = A,T,C or G

<400> 396

```
tggagttntc agtgcacaaca agccataaag cttcagtagc aaattactgt ctcacagaaa 60
gacattttca acttctgctc cagctgctga taaaacaaat catgtgttta gcttgactcc 120
agacaaggac aacctgttcc ttcataactc tctagagaaa aaaaggagtt gttagtagat 180
actaaaaaaa gtggatgaat aatctggata tttttcctaa aaagattcct tgaaacacat 240
taggaaaatg gagggcctta tgatcagaat gctagaatta gtccattgtg ctgaagcagg 300
gtttagggga gggagtggag gataaaagaa ggaaaaaag aagagtgaga aaacctattt 360
atcaaagcag gtgctatcac tcaatgttag gccctgctct ttt 403
```

<210> 397

<211> 100

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(100)

<223> n = A,T,C or G

<400> 397

```
actagtnacg tgtggtggaa ttcgcggccg cgctgacctc naanccatct ctatagcaaa 60
tccatccccg ctcttggttg gtnacagaat gactgacaaa 100
```

<210> 398

<211> 278

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(278)

<223> n = A,T,C or G

<400> 398

```
gcggccgcgt cgacagcagt tccgccagcg ctgcacctg ggtggggatg tgctgcacgc 60
ccacctggac atctggaagt cagcggcctg gatgaaagag cggacttcac ctggggcgat 120
tcactactgt gcctcgacca gtgaggagag ctggaccgac agcgaggtgg actcatcatg 180
```

138

ctccgggag cccatccacc tgtggcagtt cctcaaggag ttgctactca agccccacag 240  
 ctagggccgc ttcattangt ggctcaacaa ggagaagg 278

<210> 399

<211> 298

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(298)

<223> n = A,T,C or G

<400> 399

acggagggtg aggaagcgnc cctgggatcg anaggatggg tctcgnatt gaccncctcn 60  
 ggggtgccng catggagcgc atgggcgcgg gcctgggcca cggcatggat cgcgtgggct 120  
 ccgagatcga gcgcatgggc ctggatcatg accgcatggg ctccgtggag cgcgtgggct 180  
 ccggcattga gcgcatgggc ccgctgggcc tcgaccacat ggcctccanc attgancgca 240  
 tgggccagac catggagcgc attggctctg gcgtggagcn catgggtgcc ggcgtggg 298

<210> 400

<211> 548

<212> DNA

<213> Homo sapiens

<400> 400

acatcaacta cttcctcatt ttaaggatcg gcagttccct tcatccctt ttcctgcctt 60  
 gtacatgtac atgtatgaaa tttccttctc ttaccgaact ctctccacac atcacaagg 120  
 caaagaacca cagccttaga agggtaagag ggcaccctat gaaatgaaat ggtgattct 180  
 tgagtctctt tttccacgt ttaaggggcc atggcaggac ttagagttgc gaggtaagac 240  
 tgcagagggc tagagaatta tttcatacag gctttgaggc caccatgtc acttatcccg 300  
 tataccctct caccatcccc ttgtctactc tgatgcccc aagatgcaac tgggcagcta 360  
 gttggcccca taattctggg cctttgttgt ttgttttaac tacttgggca tcccaggga 420  
 cttccagtg atctcctacc atgggcccc ctcctgggat caagcccctc ccaggccctg 480  
 tccccagccc ctctgcccc agcccacccg cttgccttg tgctcagccc tccattggg 540  
 agcagggtt 548

<210> 401

<211> 355

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(355)

<223> n = A,T,C or G

<400> 401

actgtttcca tggtatgttt ctacacattg ctacctcagt gctcctggaa acttagcttt 60  
 tgatgtctcc aagtagtcca ccttcattta actctttgaa actgtatcat ctttgccaag 120  
 taagagtggg gccctatttc agctgctttg acaaaatgac tggctcctga cttacgttc 180  
 tataaatgaa tgtgctgaag caaagtgcc atgggtggcg cgaagaagan aaagatgtgt 240  
 tttgttttgg actctctgtg gtcccttcca atgctgnggg tttccaacca ggggaagggt 300  
 cccttttgc tggccaagt ccataacat gagcactact ctaccatggn tctgc 355

<210> 402

<211> 407

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(407)

<223> n = A,T,C or G

<400> 402

```
atggggcaag ctggataaag aaccaagacc cactggagta tgctgtcttc aagaaaccca 60
tctcacatgc ggtggcatac ataggctcaa aataaaggaa tggagaaaaa tatttcaagc 120
aaatggaaaa cagaaaaaag cagggtgttc actcctactt tctgacaaaa cagactatgc 180
gaataaagat aaaaaagaga aggacattac aaagggtggtc ctgacctttg ataatctca 240
ttgcttgata ccaacctggg ctgttttaat tgcccaaacc aaaaggataa ttgctgagg 300
ttgtggagct tctccctgc agagagtccc tgatctccca aaatttggtt gagatgtaag 360
gntgattttg ctgacaactc cttttctgaa gttttactca tttccaa 407
```

<210> 403

<211> 303

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(303)

<223> n = A,T,C or G

<400> 403

```
cagtatttat agccnaactg aaaagctagt agcaggcaag tctcaaatcc aggcacacaa 60
tcctaagcaa gagcctatggc atggtgaaaa tgcaaaagga gagtctggcc aatctacaaa 120
tagagaacaa gacctactca gtcattgaaca aaaaggcaga caccaacatg gatctcatgg 180
gggattggat attgtaatta tagagcagga agatgacagt gatcgtcatt tggcacaaca 240
tcttaacaac gaccgaaacc cattatttac ataaacctcc attcggtaac catgttgaaa 300
gga 303
```

<210> 404

<211> 225

<212> DNA

<213> Homo sapiens

<400> 404

```
aagtgtact tttaaaaatt tagtggattt tgaaaattct tagaggaaag taaaggaaaa 60
attgttaatg cactcattta cttttacatg gtgaaagtcc tctcttgatc ctacaaacag 120
acattttcca ctctgttttc catagtgttt aagtgtatca gatgtgttgg gcatgtgaat 180
ctccaagtgc ctgtgtaata aataaagtat ctttatttca ttcat 225
```

<210> 405

<211> 334

<212> DNA

<213> Homo sapiens

<220>

<221> misc\_feature

<222> (1)...(334)

<223> n = A,T,C or G

<400> 405

```
gagctgttat actgtgagtt ctactaggaa atcatcaaat ctgagggttg tctggaggac 60
ttcaatacac ctccccccat agtgaatcag cttccagggg gtccagtccc tctccttact 120
```

140

```

tcattcccat cccatgccaa aggaagaccc tccctccttg gctcacagcc ttctctaggc 180
ttccagtgct ctccaggaca gagtgggtta tgttttcagc tccatccttg ctgtgagtgt 240
ctggtgcggt tgtgcctcca gcttctgctc agtgcttcat ggacagtgtc cagcccatgt 300
cactctccac tctctcannn tggatccac ccct 334

```

<210> 406  
 <211> 216  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(216)  
 <223> n = A,T,C or G

```

<400> 406
tttcatacct aatgagggag ttganatnac atnnaaccag gaaatgcatg gatctcaang 60
gaaacaaaca cccaataaac tcggagtggc agactgacaa ctgtgagaca tgcacttgct 120
acnaaacaca aatttnatgt tgcacccttg tttctacacc tgtgggttat gacaaagaca 180
actgccaag aatnttcaag aaggaggact gccant 216

```

<210> 407  
 <211> 413  
 <212> DNA  
 <213> Homo sapiens

```

<400> 407
gctgacttgc tagtatcatc tgcattcatt gaagcacaag aacttcatgc cttgactcat 60
gtaaatgcaa taggattaaa aaataaattt gatatcacat ggaaacagac aaaaaatatt 120
gtacaacatt gcacccagtg tcagattcta cacctggcca ctcaggaagc aagagttaat 180
cccagaggct tatgtcctaa tgtgttatgg caaatggatg tcatgcaagt accttcattt 240
ggaaaattgt catttgtcca tgtgacagtt gatacttatt cacatttcat atgggcaacc 300
tgccagacag gagaaagtct tcccatgtta aaagacattt attatcttgt tttcctgtca 360
tgggagttcc agaaaaagtt aaaacagaca atgggccagg ttctgtagta aag 413

```

<210> 408  
 <211> 183  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(183)  
 <223> n = A,T,C or G

```

<400> 408
ggagctngcc ctcaattcct ccatntctat gttancatat ttaatgtctt ttgnnatata 60
tncttaacta gttaatcctt aaagggtan ntaatcctta actagtccct ccattgtgag 120
cattatcctt ccagtattcn ccttctnttt tatttactcc ttcttggtta cccatgtact 180
ntt 183

```

<210> 409  
 <211> 250  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature

141

&lt;222&gt; (1)...(250)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 409

```

cccacgcacg ataagctctt tattttctgta agtcctgcta ggaaatcatc aaatctgacg 60
gtggttttgg ggacctgaac aaacctcctg taattaatca gctttcagtt tctcccccta 120
gtccctcctt caacaacata ggaggatcct ccccttcttt ctgctcacgg ccttatctag 180
gcttccaggt gccccagga cagcgtgggc tatgtttaca gcgntcctt gctggggggg 240
ggcctatgc                                     250

```

&lt;210&gt; 410

&lt;211&gt; 306

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(306)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 410

```

ggctggtttg caagaatgaa atgaatgatt ctacagctag gacttaacct tgaaatggaa 60
agtcttgcaa tccattttgc aggatccgtc tgtgcacatg cctctgtaga gagcagcatt 120
cccaggagacc ttggaacag ttggcactgt aagggtgctt ctccccaaga cacatcctaa 180
aagggtgttg aatgggtgaaa accgcttcct tctttattgc cccttcttat ttatgtgaac 240
nactggttgg ctttttttgn atctttttta aactggaaag ttcaattgng aaaatgaata 300
tcntgc                                     306

```

&lt;210&gt; 411

&lt;211&gt; 261

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(261)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 411

```

agagatattn cttaggtnaa agttcataga gttcccatga actatatgac tggccacaca 60
ggatcttttg tatttaagga ttctgagatt ttgcttgagc aggattagat aaggctgttc 120
tttaaagtgc tgaaatggaa cagatttcaa aaaaaaaccc cacaatctag ggtgggaaca 180
aggaaggaaa gatgtgaata ggctgatggg caaaaacca atttaccat cagttccagc 240
cttctctcaa gngaggcaa a                                     261

```

&lt;210&gt; 412

&lt;211&gt; 241

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(241)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 412

```

gttcaatggt acctgacatt tctacaacac cccactcacc gatgtattcg ttgcccagtg 60
ggaacatacc agcctgaatt tggaaaaaat aattgtgttt cttgccagc aaatactacg 120

```

142

actgactttg atggctccac aaacataacc cagtgtaaaa acagaagatg tggaggggag 180  
ctgggagatt tcaactggga cattgaattc ccaactacc cangcaatta cccagccaac 240  
a 241

<210> 413  
<211> 231  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(231)  
<223> n = A,T,C or G

<400> 413  
aactcttaca atccaagtga ctcatctgtg tgcttgaatc ctttccactg tctcatctcc 60  
ctcatccaag tttctagtac cttctctttg ttgtgaagga taatcaaact gaacaacaaa 120  
aagtttactc tcctcatttg gaacctaaaa actctcttct tcctgggtct gagggctcca 180  
agaatccttg aatcanttct cagatcattg gggacaccan atcaggaacc t 231

<210> 414  
<211> 234  
<212> DNA  
<213> Homo sapiens

<400> 414  
actgtccatg aagcactgag cagaagctgg aggcacacac caccagacac tcacagcaag 60  
gatggagctg aaaacataac ccactctgtc ctggaggcac tgggaagcct agagaaggct 120  
gtgagccaag gagggagggt cttccttttg catgggatgg ggatgaagta aggagagggg 180  
ctggaccccc tggaagctga ttcactatgg ggggagggtg attgaagtcc tcca 234

<210> 415  
<211> 217  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(217)  
<223> n = A,T,C or G

<400> 415  
gcataggatt aagactgagt atcttttcta cattctttta actttctaag gggcacttct 60  
caaaacacag accaggtagc aaatctccac tgctctaagg ntctcaccac cactttctca 120  
cacctagcaa tagtagaatt cagtcctact tctgaggcca gaagaatggt tcagaaaaat 180  
antggattat aaaaaataac aattaagaaa aataatc 217

<210> 416  
<211> 213  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(213)  
<223> n = A,T,C or G

<400> 416

143

```

atgcataatnt aaagganact gcctcgcttt tagaagacat ctggngctgct ctctgcatga 60
ggcacagcag taaagctctt tgattcccag aatcaagaac tctccccttc agactattac 120
cgaatgcaag gtgggtaatt gaaggccact aattgatgct caaatagaag gatattgact 180
atattggaac agatggagtc tctactacaa aag                                     213

```

```

<210> 417
<211> 303
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(303)
<223> n = A,T,C or G

```

```

<400> 417
nagtcttcag gcccatcagg gaagttcaca ctggagagaa gtcatacata tgtactgtat 60
gtgggaaagg ctttactctg agttcaaadc ttcaagccca tcagagagtc cactactggag 120
agaagccata caaatgcaat gagggtggga agagcttcag gagggtattcc cattatcaag 180
ttcatctagt ggtccacaca ggagagaaaac cctataaatg tgagatatgt gggaagggt 240
tcantcaaaag ttcgtatctt caaatccatc ngaagggncca cagtatanan aaacctttta 300
agt                                     303

```

```

<210> 418
<211> 328
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(328)
<223> n = A,T,C or G

```

```

<400> 418
tttttgccgg tgggtgggga gggacgggac angagtctca ctctgttgcc caggctggag 60
tgacacaggca tgatctcggc tcaactacaac ccctgcctcc catgtccaag cgattcttgt 120
gcctcagcct tcctctgtagc tagaattaca ggcacatgcc accacaccca gctagttttt 180
gtatttttag tagagacagg gtttcacat gttggccagg ctggtctcaa actcctnacc 240
tcagnggtca ggctgggtc aaactcctga cctcaagtga tctgcccacc tcagcctccc 300
aaagtgtan gattacaggc cgtgagcc                                     328

```

```

<210> 419
<211> 389
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(389)
<223> n = A,T,C or G

```

```

<400> 419
cctcctcaag acggcctgtg gtccgcctcc cggcaaccaa gaagcctgca gtgccatag 60
acccttgagc catggactgg agcctgaaag gcagcgtaca ccctgctcct gatcttctgt 120
ctgttttct ctctgtggct ccattcatag cacagtgtgt gactgaggc ttgtgcaggc 180
cgagcaaggc caagctggct caaagagcaa ccagtcaact ctgccacggg gtgccaggca 240
ccggttctcc agccaccaac ctcaactgct cccgcaaagt gcacatcagt tcttctacc 300
taaaggtagg accaaagggc atctgctttt ctgaagtcct ctgctctatc agccatcacg 360

```



144

tggcagccac tcnggctgtg tcgacgagg

389

&lt;210&gt; 420

&lt;211&gt; 408

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 420

gttcctccta actcctgcc aaaaacagctc tcctcaacat gagagctgca cccctcctcc 60  
tggccagggc agcaagcctt agccttggct tcttgtttct gctttttttc tggctagacc 120  
gaagtgtact agccaaggag ttgaagtttg tgacttttgt gtttcggcat ggagaccgaa 180  
gtcccattga cacttttccc actgacccca taaaggaatc ctcatggcca caaggatttg 240  
gccaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaga 300  
gatatagaaa attccttgaat gactcctata aacatgaaca ggtttatatt cgaagcacag 360  
acgttgaccg gactttgatg aagtgcctatg acaaacctgg caagcccg 408

&lt;210&gt; 421

&lt;211&gt; 352

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(352)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 421

gctcaaaaat ctttttactg atnggcatgg ctacacaatc attgactatt acggaggcca 60  
gaggagaatg aggcctggcc tgggagccct gtgcctacta naagcacatt agattatcca 120  
ttcactgaca gaacaggctc tttttgggtc cttcttctcc accacnatac acttgcatgc 180  
ctccttcttg aagattcttt ggcagttgtc tttgtcataa cccacaggtg tagaaacaag 240  
ggtgcaacat gaaatttctg tttcgtagca agtgcattgc tcacaagttg gcangtctgc 300  
cactccgagt ttattgggtg tttgtttcct ttgagatcca tgcatttcct gg 352

&lt;210&gt; 422

&lt;211&gt; 337

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 422

atgccaccat gctggcaatg cagcggggcg tcgaaggcct gcataatccag cccaagctgg 60  
cgatgatcga cggcaaccgt tgcccgaagt tgccgatgcc agccgaagcg gtggtcaagg 120  
gcgatagcaa ggtgccggcg atcgccggcg cgtcaatcct ggccaaggtc agccgtgac 180  
gtgaaatggc agctgtcgaa ttgatctacc cgggttatgg catcgccggg cataagggct 240  
atccgacacc ggtgcacctg gaagccttgc agcggctggg gccgacgccg attcaccgac 300  
gcttcttccg ccggtacggc tggcctatga aaattat 337

&lt;210&gt; 423

&lt;211&gt; 310

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(310)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 423

145

```

gctcaaaaat ctttttactg atatggcatg gctacacaat cattgactat tagaggccag 60
aggagaatga ggcctggcct gggagccctg tgcctactan aagcncatta gattatccat 120
tactgacag aacaggtctt ttttgggtcc ttcttctcca ccacgatata ctgacgtcc 180
tccttcttga agattctttg gcagttgtct ttgtcataac ccacaggtgt anaaacaagg 240
gtgcaacatg aaatttctgt ttcgtagcaa gtgcatgtct cacagttgtc aagtctgccc 300
tccgagttta                                     310

```

```

<210> 424
<211> 370
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(370).
<223> n = A,T,C or G

```

```

<400> 424
gctcaaaaat ctttttactg ataggcatg ctacacaatc attgactatt agaggccaga 60
ggagaatgag gctggcctg ggagccctgt gcctactaga agcacattag attatccatt 120
cactgacaga acaggtcttt tttgggtcct tcttctccac cacgatatac ttgcagtcc 180
ccttcttgaa gattcttttg cagttgtctt tgtcataacc cacaggtgta gaaacatcct 240
ggttgaatct cctggaactc cctcattagg tatgaaatag catgatgcat tgcataaagt 300
cacgaaggtg gcaaagatca caacgctgcc cagganaaca ttcattgtga taagcaggac 360
tccgtcgacg                                     370

```

```

<210> 425
<211> 216
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(216)
<223> n = A,T,C or G

```

```

<400> 425
aattgctatn ntttattttg ccactcaaaa taattaccaa aaaaaaaaaa tnttaaatga 60
taacaacnca acatcaaggn aaananaaca ggaatggntg actntgcata aatnggccga 120
anattatcca ttatnttaag ggttgacttc aggntacagc acacagacaa acatgccag 180
gaggntntca ggaccgctcg atgtntntng aggagg                                     216

```

```

<210> 426
<211> 596
<212> DNA
<213> Homo sapiens

```

```

<400> 426
cttccagtga ggataaccct gttgccccgg gccgaggttc tccattaggc totgattgat 60
tggcagtcag tgatggaagg gtgttctgat cattccgact gcccgaaggg tcgctggcca 120
gctctctgtt ttgtcgagtt ggcagtagga cctaatttgt taattaagag tagatgggtga 180
gctgtccttg tattttgatt aacctaatgg ccttcccagc acgactcgga ttcagctgga 240
gacatcacgg caacttttaa tgaaatgatt tgaagggccca ttaagaggca cttcccgta 300
ttaggcagtt catctgcact gataacttct tggcagctga gctggtcgga gctgtggccc 360
aaacgcacac ttggcttttg gttttgagat acaactctta atcttttagt catgcttgag 420
ggtggatggc cttttcagct ttaacccaat ttgcaactgc ttggaagtgt agccaggaga 480
atacactcat atactcgtgg gcttagaggc cacagcagat gtcattggtc tactgcctga 540
gtcccgcgtg tcccatccca ggaccttcca tcggcgagta cctgggagcc cgtgct 596

```

146

<210> 427  
<211> 107  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(107)  
<223> n = A,T,C or G

<400> 427  
gaagaattca agttaggttt attcaaaggg cttacngaga atcctanacc caggncaccag 60  
cccgggagca gccttanaga gctcctgttt gactgcccgg ctcagn 107

<210> 428  
<211> 38  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(38)  
<223> n = A,T,C or G

<400> 428  
gaacttcna anaangactt tattcactat ttacatt 38

<210> 429  
<211> 544  
<212> DNA  
<213> Homo sapiens

<400> 429  
ctttgctgga cggaataaaa gtggacgcaa gcatgacctc ctgatgaggg cgctgcattt 60  
attgaagagc ggctgcagcc ctgcggttca gattaaaatc cgagaattgt atagacgccg 120  
atatccacga actcttgaag gactttctga tttatccaca atcaaatcat cggttttcag 180  
tttgatgggt ggctcatcac ctgtagaacc tgacttggcc gtggctggaa tccactcggt 240  
gccttccact tcagttacac ctcactcacc atcctctcct gttggtctg tgcgtcttca 300  
agatactaag cccacatttg agatgcagca gccatctccc ccaattcctc ctgtccatcc 360  
tgatgtgcag ttaaaaaatc tgccctttta tgatgtcctt gatgttctca tcaagccac 420  
gagtttagtt caaagcagta ttcagcgatt tcaagagaag ttttttattt ttgctttgac 480  
acctcaaca gttagagaga tatgcatatc cagggtttt ttgccagggt gtaggagaga 540  
ttat 544

<210> 430  
<211> 507  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(507)  
<223> n = A,T,C or G

<400> 430  
cttatacnaa tggggctccc aaacttggct gtgcagtga aactccgggg gaattttgaa 60  
gaacactgac acccatcttc caccocgaca ctctgattta attgggctgc agtgagaaca 120

147

```

gagcatcaat ttaaaaagct gccagaatg ttntcctggg cagcgttggt atctttgccn 180
ccttcgtgac tttatgcaat gcatcatgct atttcatacc taatgaggga gttccaggag 240
attcaaccag gatgtttcta cncctgtggg ttatgacaaa gacaactgcc aaagaatntt 300
caagaaggag gactgcaagt atatcgtggg ggagaagaag gacccaaaaa agacctgttc 360
tgtcagtga tggataatct aatgtgcttc tagtaggcac agggctccca gccaggcct 420
cattctctc tggcctctaa tagtcaatga ttgtgtagcc atgcctatca gtaaaaagat 480
ttttgagcaa aaaaaaaaaa aaaaaaa 507

```

```

<210> 431
<211> 392
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(392)
<223> n = A,T,C or G

```

```

<400> 431
gaaaattcag aatggataaa aacaaatgaa gtacaaaata ttccagattt acatagcgat 60
aaacaagaaa gcacttatca ggaggactta caaatggaag taaactctan aaccatcatc 120
tatcatggct aaatgtgaga ttagcacagc tgtattatit gtacattgca aacacctaga 180
aagagatggg aaacaaaatc ccaggagttt tgtgtgtgga gtccctgggt ttccaacaga 240
catcattcca gcattctgag attagggnga ttggggatca ttctggagtt ggaatgttca 300
acaaaagtga tgttgttagg taaaatgtac aacttctgga tctatgcaga cattgaaggt 360
gcaatgagtc tggcttttac tctgctgttt ct 392

```

```

<210> 432
<211> 387
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(387)
<223> n = A,T,C or G

```

```

<400> 432
ggtatccnta cataatcaaa tatagctgta gtacatgttt tcattgngt agattaccac 60
aaatgcaagg caacatgtgt agatctcttg tcttattctt ttgtctataa tactgtattg 120
ngtagtccaa gctctcggna gtccagccac tngaaacat gctcccttta gattaacctc 180
gtggacnctn ttgttgnatt gtctgaactg tagngccctg tattttgctt ctgtctgnga 240
attctgttgc ttctggggca ttctcttng atgcagagga ccaccacaca gatgacagca 300
atctgaattg ntccaatcac agctgcgatt aagacatact gaaatcgtac aggaccggga 360
acaacgtata gaacactgga gtccttt 387

```

```

<210> 433
<211> 281
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(281)
<223> n = A,T,C or G

```

```

<400> 433
ttcaactagc anagaanact gcttcagggn gtgtaaaatg aaaggcttcc acgcagttat 60

```

148

```

ctgattaaag aacactaaga gagggacaag gctagaagcc gcaggatgtc tacactatag 120
caggcncctat ttgggttggc tggaggagct gtggaaaaca tggagagatt ggcgctggag 180
atcgccgtgg ctattcctcn ttgntattac accagnaggg ntctctgtnt gccactggg 240
tnnaaacccg ntatacaata atgatagaat aggacacaca t 281

```

```

<210> 434
<211> 484
<212> DNA
<213> Homo sapiens

```

```

<400> 434
ttttaaaata agcatttagt gctcagtcct tactgagtac tctttctctc cctcctctgt 60
aatttaattc tttcaacttg caatttgcaa ggattacaca tttactgtg atgtatatg 120
tgttgcaaaa aaaaaaaagt gtctttgttt aaaattactt ggtttggtga tccatcttgc 180
tttttcccca ttggaactag tcattaaccc atctctgaac tggtagaaaa acatctgaag 240
agctagtcta tcagcatctg acaggtgaat tggatgggtc tcagaacctt ttcaccaga 300
cagcctgttt ctatcctgtt taataaatta gtttgggttc tctacatgca taacaaaccc 360
tgctccaatc tgtcacataa aagtctgtga cttgaagttt agtcagcacc cccaccaaac 420
tttatttttc tatgtgtttt ttgcaacata tgagtgtttt gaaaataaag taccatgtc 480
ttaa 484

```

```

<210> 435
<211> 424
<212> DNA
<213> Homo sapiens

```

```

<400> 435
gcgcgcgtca gacgaggtca ctttctgcct tccacgtcct ccttcaagga agccccatgt 60
gggtagcttt caatatcgca ggttcttact cctctgcctc tataagctca aaccaccaa 120
cgatcgggca agtaaacccc ctccctcgcc gacttcggaa ctggcgagag ttcagcgag 180
atgggcctgt ggggaggggg caagatagat gagggggagc ggcatgggtc ggggtgacct 240
cttgagagaga gaaaaaaggc cacaagaggg gctgccaccg ccactaacgg agatggccct 300
ggtagagacc tttgggggtc tggaacctct ggactcccca tgctctaact cccacactct 360
gctatcagaa acttaaaactt gaggattttc tctgtttttc actcgcaata aattcagagc 420
aaac 424

```

```

<210> 436
<211> 667
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(667)
<223> n = A,T,C or G

```

```

<400> 436
accttgggaa nactctcaca atataaaggg tcgtagactt tactccaaat tccaaaaagg 60
tcctggccat gtaatcctga aagttttccc aaggtagcta taaaatcett ataaggggtc 120
agcctcttct ggaattctc tgatttcaaa gtctcactct caagttcttg aaaacgaggg 180
cagttcctga aaggcaggt tagcaactga tcttcagaaa gaggaactgt gtgcaccggg 240
atgggctgcc agagtaggat aggattccag atgtgacac cttctggggg aaacaggggt 300
gccaggtttg tcatagcact catcaaagtc cggtaacgt ctgtgcttcg aatataaacc 360
tgttcatgtt tataggactc attcaagaat tttctatatc tctttcttat atactctcca 420
agttcataat gctgctccat gccagctgg gtgagttggc caaatccttg tggccatgag 480
gattccttta tggggtcagt gggaaagggt tcaatgggac ttcggtctcc atgccgaaac 540
accaaagtca caaacttcaa ctcttgggt agtacacttc ggtctagcca gaaaaaagg 600
agaaacaaga agccaaggct aaggcttgct gccctgccag gaggggggt gcagctctca 660

```

149

tgttgag

667

&lt;210&gt; 437

&lt;211&gt; 693

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 437

```
ctacgtctca accctcattt ttaggtaagg aatcttaagt ccaaagatat taagtgactc 60
acacagccag gtaaggaaag ctggattggc acactaggac tctaccatac cgggttttgt 120
taaagctcag gttaggaggc tgataagctt ggaaggaaact tcagacagct ttttcagatc 180
ataaaagata attcttagcc catgttcttc tccagagcag acctgaaatg acagcacagc 240
aggctactcct ctattttcac ccctcttgct tctactctct ggcagtcaga cctgtgggag 300
gccatgggag aaagcagctc tctggatggt tgtacagatc atggactatt ctctgtggac 360
cattttctcca ggttacccta ggtgtcacta ttggggggac agccagcatc tttagctttc 420
atttgagttt ctgtctgtct tcagtagagg aaacttttgc tottcacact tcacatctga 480
acacctaaact gctgttgctc ctgaggtggg gaaagacaga tatagagctt acagtattta 540
tcctatttct aggcactgag ggctgtgggg taccttgtgg tgccaaaaca gatcctgttt 600
taaggacatg ttgcttcaga gatgtctgta actatctggg ggctctgttg gctctttacc 660
ctgcatcatg tgctctcttg gctgaaaatg acc 693
```

&lt;210&gt; 438

&lt;211&gt; 360

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 438

```
ctgcttatca caatgaatgt tctcctgggc agcgttgtga tctttgccac ctctgtgact 60
ttatgcaatg catcatgcta tttcatacct aatgagggag ttccaggaga ttcaaccagg 120
atgtttctac acctgtgggt tatgacaaag acaactgcc aagaatcttc aagaaggagg 180
actgcaagta tatctgttg agaagaagga cccaaaaaag acctgttctg tcagtgaatg 240
gataatctaa tgtgttcta gtaggcacag ggctcccagg ccaggcctca ttctcctctg 300
gcctctaata gtcaataatt gtgtagccat gcctatcagt aaaaagattt ttgagcaaac 360
```

&lt;210&gt; 439

&lt;211&gt; 431

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(431)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 439

```
gttcctnnta actcctgcc aaaaacagctc tcctcaacat gagagctgca cccctcctcc 60
tgccagggc agcaagcctt agccttggt tcttgtttct gcttttttct tggctagacc 120
gaagtgtact agccaaggag ttgaagtttg tgactttggt gtttcggcat ggagaccgaa 180
gtcccattga cacttttccc actgacccca taaaggaatc ctcatggcca caaggatttg 240
gccaaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaga 300
gatatagaaa attcttgaat gagtccata aacatgaaca ggtttatatt cgaagcacag 360
acgttgaccg gactttgatg agtgcetatg caaacctggc agcccgctga cgcggccgcg 420
aathtagtag t 431
```

&lt;210&gt; 440

&lt;211&gt; 523

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

150

<400> 440  
 agagataaag cttaggtcaa agttcataga gttcccatga actatatgac tggccacaca 60  
 ggatcttttg tatttaagga ttctgagatt ttgcttgagc aggattagat aaggctgttc 120  
 tttaaatgtc tgaaatggaa cagatttcaa aaaaaaaccc cacaatctag ggtgggaaca 180  
 aggaaggaaa gatgtgaata ggctgatggg caaaaaacca atttaccat cagttccagc 240  
 cttctctcaa ggagaggcaa agaaaggaga tacagtggag acatctggaa agttttctcc 300  
 actggaaaac tgctactatc tgtttttata tttctgttaa aatatatgag gctacagaac 360  
 taaaaaattaa aacctctttg tgtcccttgg tcttggaaaca tttatgttcc ttttaaagaa 420  
 acaaaaatca aactttacag aaagatttga tgtatgtaat acatatagca gctcttgaag 480  
 tatatatatc atagcaaata agtcactctga tgagaacaag cta 523

<210> 441  
 <211> 430  
 <212> DNA  
 <213> Homo sapiens

<400> 441  
 gttcctccta actcctgcc aaaacagctc tctcaacat gagagctgca cccctcctcc 60  
 tggccagggc agcaagcctt agccttggct tcttgtttct gcttttttcc tggctagacc 120  
 gaagtgtact agccaaggag ttgaagtttg tgactttggg gtttcggcat ggagaccgaa 180  
 gtcccattga cacttttccc actgacccca taaaggaatc ctcattggcca caaggatttg 240  
 gccaaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaga 300  
 gatatagaaa attccttgaat gagtcctata aacatgaaca ggtttatatt cgaagcacag 360  
 acgttgaccg gactttgatg agtgctatga caaacctggc agcccgtcga cgccggccgcg 420  
 aatttagtag 430

<210> 442  
 <211> 362  
 <212> DNA  
 <213> Homo sapiens

<400> 442  
 ctaaggaatt agtagtgttc ccatcacttg tttggagtgt gctattctaa aagattttga 60  
 tttcctggaa tgacaattat attttaactt tgggtgggga aagagttata ggaccacagt 120  
 cttcacttct gatacttgta aattaatctt ttattgcact tgttttgacc attagctat 180  
 atgttttagaa atggtcattt tacggaaaaa ttagaaaaat tctgataata gtgcagaata 240  
 aatgaattaa tgttttactt aatttatatt gaactgtcaa tgacaaataa aaattctttt 300  
 tgattatttt ttgttttcat ttaccagaat aaaaactaag aattaaaagt ttgattacag 360  
 tc 362

<210> 443  
 <211> 624  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(624)  
 <223> n = A,T,C or G

<400> 443  
 tttttttttt gcaacacaa atacatcaca gtgaaatgtg taatccttgc aaattgcaag 60  
 ttgaaagaat taaattcaga ggaggggaga gaaagagtag tcagtaggga ctgagcacta 120  
 aatgcttatt ttaaagaaa tgtaaagagc agaaagcaat tcaggctacc ctgccttttg 180  
 tgcgtggctag tactccggtc ggtgtcagca gcacgtggca ttgaacattg caatgtggag 240  
 cccaaaccac agaaaatggg gtgaaattgg ccaactttct attaacttgg cttcctgttt 300  
 tataaaatat tgtgaataat atcacctact tcaaagggca gttatgaggc ttaaatgaac 360

151

```

taacgcctac aaaacactta aacatagata acataggtgc aagtactatg tatctggtac 420
atggttaaaca tccttattat taaagtcaac gctaaaatga atgtgtgtgc atagctaat 480
agtcagaga gagggcactt aaaccaacta agggcctgga gggaaggttt cctggaaaga 540
ngatgcttgt gctgggtcca aatcttggtc tactatgacc ttggccaaat tatttaaact 600
ttgccctat ctgctaaaca gatc 624

```

```

<210> 444
<211> 425
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(425)
<223> n = A,T,C or G

```

```

<400> 444
gcacatcatt nntcttgcatt tctttgagaa taagaagatc agtaaatagt tcagaagtgg 60
gaagctttgt ccaggcctgt gtgtgaaccc aatgttttgc ttagaaatag aacaagtaag 120
ttcattgcta tagcataaca caaaatttgc ataagtgggtg gtcagcaaat ccttgaatgc 180
tgcttaattgt gagaggttgg taaaatcctt tgtgcaacac tctaactccc tgaatgtttt 240
gctgtgctgg gacctgtgca tgccagacaa ggccaagctg gctgaaagag caaccagcca 300
cctctgcaat ctgccacctc ctgctggcag gatttgtttt tgcactcctgt gaagagccaa 360
ggaggcacca gggcataagt gagtagactt atggtcgacg cggccgcgaa ttagtagtagta 420
gtaga 425

```

```

<210> 445
<211> 414
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(414)
<223> n = A,T,C or G

```

```

<400> 445
catgtttatg nttttggatt actttgggca cctagtgttt ctaaatacgtc tatcattcctt 60
ttctgttttt caaaagcaga gatggccaga gtctcaacaa actgtatcctt caagtctttg 120
tgaaattcctt tgcatgtggc agattatttg atgtagtttc ctttaactag catataaatc 180
tggtgtgttt cagataaatg aacagcaaaa tgtggtggaa ttaccatttg gaacattgtg 240
aatgaaaaat tgtgtctcta gattatgtaa caaataacta tticctaacc attgatcttt 300
ggatttttat aatcctactc acaaatagact aggtctctcc tcttgtattt tgaagcagtg 360
tgggtgctgg attgataaaa aaaaaaaaag tcgacgcggc cggaatttta gtag 414

```

```

<210> 446
<211> 631
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(631)
<223> n = A,T,C or G

```

```

<400> 446
acaaattaga anaaagtgcc agagaacacc acataccttg tccggaacat tacaatggct 60
tctgcatgca tgggaagtgt gagcattcta tcaatatgca ggagccatct tgcaggtgtg 120

```



152

```

atgctgggta tactggacaa cactgtgaaa aaaaggacta cagtgttcta tacgttggtc 180
ccggtcctgt acgatttcag tatgtcttaa tcgcagctgt gattggaaca attcagattg 240
ctgtcatctg tgtgggtggc ctctgcatca caagggccaa actttaggta atagcattgg 300
actgagattt gtaaaccttc caaccttcca ggaaatgccc cagaagcaac agaattcaca 360
gacagaagca aaatacaggg cactacagtt cagacaatac aacaagagcg tccacgaggt 420
taatctaaag ggagcatgtt tcacagtggc tggactaccg agagcttgga ctacacaata 480
cagtattata gacaaaagaa taagacaaga gatctacaca tgttgccctg catttgtggt 540
aatctacacc aatgaaaaca tgtactacag ctatatattga ttatgtatgg atatatattga 600
aatagtatac attgtcttga tgttttttct g                                     631

```

<210> 447  
 <211> 585  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(585)  
 <223> n = A,T,C or G

```

<400> 447
ccttgggaaa antntcacaa tataaagggt cgtagacttt actccaaatt ccaaaaagggt 60
cctggccatg taatcctgaa agttttccca aggtagctat aaaatcctta taagggtgca 120
gcctcttctg gaattcctct gatttcaaag tctcactctc aagttcttga aaacgagggc 180
agttcctgaa aggcagggtat agcaactgat cticagaaag aggaactgtg tgcaccggga 240
tgggctgcca gagtaggata ggattccaga tgctgacacc ttctggggga aacagggtcg 300
ccagggttgt catagcactc atcaaagtcc ggtcaacgtc tgtgcttcga atataaacct 360
gttcatgttt ataggactca ttcaagaatt ttctatatct ctttcttata tactctccaa 420
gttcataatg ctgctccatg cccagctggg tgagttggcc aaatccttgt ggccatgagg 480
attcctttat ggggtcagtg ggaaagggtg caatgggact tcggtctcca tgccgaaaca 540
ccaaagtcac aaacttcaac tccttggtta gtacacttcg gtcta                    585

```

<210> 448  
 <211> 93  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(93)  
 <223> n = A,T,C or G

```

<400> 448
tgctcgtggg tcattctgan nnccgaactg accntgccag ccctgccgan gggcnccat 60
ggctccctag tgccctggag agganggggc tag                               93

```

<210> 449  
 <211> 706  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(706)  
 <223> n = A,T,C or G

```

<400> 449
ccaagttcat gctntgtgct ggacgctgga cagggggcaa aagcnnttgc tcgtgggtca 60

```

```

ttctgancac cgaactgacc atgccagccc tgccgatggt cctccatggc tccctagtgc 120
cctggagag aggtgtctag tcagagagta gtccctggaag gtggcctctg ngaggagcca 180
cggggacagc atcctgcaga tggtcgggcg cgtcccattc gccattcagg ctgcgcaact 240
gttggaagg gcgatcggtg cgggcctctt cgctattacg ccagctggcg aaaggggat 300
gtgctgcaag gcgattaagt tgggtaacgc cagggttttc ccagtcncga cgttgtaaaa 360
cgacggccag tgaattgaat ttaggtgacn ctatagaaga gctatgacgt cgcattgcac 420
cgtaacgtaag cttggatcct cttagcgggc cgcctactac tactaaattc gcggccgcgt 480
cgacgtggga tccnactga gagagtggag agtgacatgt gctggacnct gtccatgaag 540
cactgagcag aagctggagg cacaacgcnc cagacactca cagctactca ggaggctgag 600
aacaggttga acctgggagg tggaggttgc aatgagctga gatcaggccn ctgcncccca 660
gcatggatga cagagtga aa ctccatctta aaaaaaaaa aaaaaa 706

```

```

<210> 450
<211> 493
<212> DNA
<213> Homo sapiens

```

```

<400> 450
gagacggagt gtcactctgt tgcccaggct ggagtgcagc aagacactgt ctaagaaaa 60
acagttttta aaggtaaaa acataaaaa gaaatatcct atagtggaaa taagagagtc 120
aaatgaggct gagaacttta caaagggatc ttacagacat gtcgccaata tcaactgcatg 180
agcctaagta taagaacaac ctttggggag aaaccatcat ttgacagtga ggtacaattc 240
caagtcaggt agtgaaatgg gtggaattaa actcaaatta atcctgccag ctgaaacgca 300
agagacactg tcagagagtt aaaaagttag ttctatccat gaggtgattc cacagtcttc 360
tcaagtcaac acatctgtga actcacagac caagttctta aacctggtt caaactctgc 420
tacacatcag aatcacctgg agagctttac aaactcccat tgccgagggc cgacgcggcc 480
gcgaatttag tag 493

```

```

<210> 451
<211> 501
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(501)
<223> n = A,T,C or G

```

```

<400> 451
gggcgcgtcc cattcgccat tcaggctgcg caactgttgg gaagggcgat cgggtcgggc 60
ctcttcgcta ttacgccagc tggcgaaagg gggatgtgct gcaaggcgat taagttgggt 120
aacgccaggg ttttccagat cncgacgttg taaaacgacg gccagtgaat tgaatttag 180
tgacnctata gaagagctat gacgtcgcat gcacgcgtac gtaagcttgg atcctctaga 240
gcggccgcct actactacta aattcgcggc cgcgtcgacg tgggatccnc actgagagag 300
tggagagtga catgtgctgg acnctgtcca tgaagcactg agcagaagct ggaggcacia 360
cgcncagac actcacagct actcaggagg ctgagaacag gttgaacctg ggaggtggag 420
gttgcaatga gctgagatca ggcnctgcn cccagcatg gatgacagag tgaaactcca 480
tcttaaaaa aaaaaaaaa a 501

```

```

<210> 452
<211> 51
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(51)
<223> n = A,T,C or G

```

154

<400> 452  
 agacgggtttc accntttacaa cnccttttag gatgggnntt ggggagcaag c 51

<210> 453  
 <211> 317  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(317)  
 <223> n = A,T,C or G

<400> 453  
 tacatcttgc tttttcccca ttggaactag tcattaaccc atctctgaac tggtagaaaa 60  
 acatctgaag agctagtcta tcagcatctg gcaagtgaat tggatggttc tcagaacccat 120  
 ttcacccana cagcctgttt ctatcctgtt taataaatta gtttgggttc tctacatgca 180  
 taacaaaccc tgctccaatc tgtcacataa aagtctgtga cttgaagttt antcagcacc 240  
 cccaccaaac tttatttttc tatgtgtttt ttgcaacata tgagtgtttt gaaaataagg 300  
 taccatgtc tttatta 317

<210> 454  
 <211> 231  
 <212> DNA  
 <213> Homo sapiens

<400> 454  
 ttcgaggtac aatcaactct cagagtgtag tttccttcta tagatgagtc agcattaata 60  
 taagccacgc cagctctctg aaggagtctt gaattctcct ctgctcactc agtagaacca 120  
 agaagaccaa attcttctgc atcccagctt gcaaacaata ttgttcttct aggtctccac 180  
 ccttctttt tcaagtgttc aaagctctc acaatttcat gaacaacagc t 231

<210> 455  
 <211> 231  
 <212> DNA  
 <213> Homo sapiens

<400> 455  
 taccaaagag ggcataataa tcagtctcac agtagggttc accatcctcc aagtgaataa 60  
 cattgttccg aatgggcttt ccacaggcta cacacacaaa acaggaaaca tgccaagttt 120  
 gtttcaacgc attgatgact tctccaagga ttttctttg gcatcgacca cattcagggg 180  
 caaagaattt ctcatagcac agctcacaat acagggtctc ttttctctct a 231

<210> 456  
 <211> 231  
 <212> DNA  
 <213> Homo sapiens

<400> 456  
 ttggcaggta cccttacaata gaagacacca taccttatgc gttattaggt ggaataatca 60  
 ttccattcag tattatcggtt attattcttg gagaaaccct gtctgtttac tgtaaccctt 120  
 tgactcaaaa ttcctttatc aggaataact acatagccac tatttacaata gccattggaa 180  
 cctttttatt tgggtgcagct gctagtcagt ccctgactga cattgccaag t 231

<210> 457  
 <211> 231  
 <212> DNA

155

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(231)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 457

```
cgaggtagcc aggggtctga aaatctctnn ttantagtc gatagcaaaa ttgttcatca 60
gcattcctta atatgatctt gctataatta gatttttctc cattagagtt catacagttt 120
tatttgattt tattagcaat ctctttcaga agacccttga gatcattaag ctttgatatc 180
agtgtgctaa atcgatgcct catttcctct gaggtgtcgc tggcttttgt g          231
```

&lt;210&gt; 458

&lt;211&gt; 231

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 458

```
aggtctgggt cccccactt ccactcccct ctactctctc taggactggg ctgggccaaag 60
agaagagggg tgggttagga agccgttgag acctgaagcc ccaccctcta ccttccttca 120
acaccctaac cttgggtaac agcatttgga attatcattt gggatgagta gaatttccaa 180
ggctctgggt taggcatttt ggggggccag accccaggag aagaagattc t          231
```

&lt;210&gt; 459

&lt;211&gt; 231

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 459

```
ggtaccgagg ctctgtgaca cagagaaacc ccaacgcgag gaaaggaatg gccagccaca 60
ccttcgcgaa acctgtggtg gcccaccagt cctaaccgga caggacagag agacagagca 120
gcctgcact gttttccctc caccacagcc atcctgtccc tcattggctc tgtgctttcc 180
actatacaca gtcacogtcc caatgagaaa caagaaggag caccctccac a          231
```

&lt;210&gt; 460

&lt;211&gt; 231

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 460

```
gcagggtataa catgctgcaa caacagatgt gactaggaac ggccggtgac atggggaggg 60
cctatcacc cttcttggg ggctgcttct tcacagtgat catgaagcct agcagcaaat 120
cccacctccc cacacgcaca cgccagcct ggagcccaca gaagggtcct cctgcagcca 180
gtggagcttg gtccagcctc cagtccaccc ctaccaggct taaggataga a          231
```

&lt;210&gt; 461

&lt;211&gt; 231

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 461

```
cgagggtttga gaagctctaa tgtgcagggg agccgagaag caggcggcct agggaggggc 60
gcgtgtgctc cagaagagt tgtgcatgcc agaggggaaa caggcgctg tgtgtcctgg 120
gtggggttca gtgaggagt ggaaattgt tcagcagaac caagccgttg ggtgaataag 180
agggggattc catggcactg atagagccct atagtctcag agctgggaat t          231
```

&lt;210&gt; 462

156

<211> 231  
<212> DNA  
<213> Homo sapiens

<400> 462  
aggtaccctc attgtagcca tgggaaaatt gatgttcagt ggggatcagt gaattaaatg 60  
gggtcatgca agtataaaaa ttaaaaaaaa aagacttcat gcccaatctc atatgatgtg 120  
gaagaactgt tagagagacc aacagggtag tgggttagag atttccagag tcttacattt 180  
tctagaggag gtatttaatt tcttctcact catccagtg tgtatttagg a 231

<210> 463  
<211> 231  
<212> DNA  
<213> Homo sapiens

<400> 463  
tactccagcc tggtagacaga gcgagaccct atcaccgccc cccacccccc caaaaaaaaa 60  
actgagtaga caggtgtcct cttggcatgg taagtcttaa gtcccctccc agatctgtga 120  
catttgacag gtgtcttttc ctctggacct cgggtgtccc atctgagtga gaaaaggcag 180  
tggggagggt gatcttccag tcgaagcggg atagaagccc gtgtgaaaag c 231

<210> 464  
<211> 231  
<212> DNA  
<213> Homo sapiens

<400> 464  
gtactctaag attttatcta agttgccttt tctgggtggg aaagttaa cttagtact 60  
aaggacatca catatgaaga atgtttaagt tggagggtgg aacgtgaatt gcaaacaggg 120  
cctgttcag tgactgtgtg cctgtagtcc cagctactcg ggagtctgtg tgaggccagg 180  
ggtgccagcg caccagctag atgctctgta acttctaggg cccattttcc c 231

<210> 465  
<211> 231  
<212> DNA  
<213> Homo sapiens

<400> 465  
catgttggt tagctgtggt aatgctggct gcatctcaga cagggttaac ttcagctcct 60  
gtggcaaatt agcaacaaat tctgacatca tatttatggt ttctgtatct ttgttgatga 120  
aggatggcac aatttttgct tgtgttcata atatactcag attagtccag ctccatcaga 180  
taaactggag acatgcagga cattagggtg gtgtgttagc tctggtaatg a 231

<210> 466  
<211> 231  
<212> DNA  
<213> Homo sapiens

<400> 466  
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<210> 467  
<211> 311  
<212> DNA  
<213> Homo sapiens

&lt;400&gt; 467

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ctgcagcaga c                                     311

```

&lt;210&gt; 468

&lt;211&gt; 3112

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 468

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&lt;210&gt; 469

&lt;211&gt; 2229

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 469

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aatggaatt 2229
```

&lt;210&gt; 470

&lt;211&gt; 2426

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 470

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&lt;210&gt; 471

&lt;211&gt; 812

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 471

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aagccatcaa gattttctcg tctgttttcc tctcattggt aatgctcact ttgtgacttc 360
atttcaaatc tgtaatcccg ttcaataaaa tatccacaac aggatctgtt ttoctgcca 420
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160

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&lt;210&gt; 472

&lt;211&gt; 515

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(515)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 472

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515

&lt;210&gt; 473

&lt;211&gt; 5829

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 473

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gaaaaagggtg	gcattgtgtt	ttactttcaa	aatattttaa	tttccatcat	tataacaaaa	4860

162

```

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aaaaaaaaa

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&lt;210&gt; 474

&lt;211&gt; 1594

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 474

```

atttatggat cattaatgcc tctttagtag tttagagaaa acgtcaaaaag aaatggcccc 60
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aaaatataaa tatatagaca tctcagataa tatatttgaa atagcaaatt cctgttagaa 180
aataatagta ctttaactaga tgagaataac aggtcgccat tatttgaatt gtctcctatt 240
cgtttttcat ttgttgtgtt actcatgttt tacttatgag ggatatatat aacttccact 300
gttttcagaa ttattgtatg cagtcagtat gagaatgcaa ttaagtttc cttgatgctt 360
tttcacactt ctattactag aaataagaat acagtaatat tggcaaagaa aattgaccag 420
ttcaataaaa ttttttagta aatctgattg aaaataaaca ttgcttatgg ctttcttaca 480
tcaatattgt tatgtcctag acaccttatt tgaaattacg gcttcaaaat tctaattatg 540
tgcaaatgtg taaaatatca atactttatg ttcaagctgg ggcctcttca ggcgtcctgg 600
gctgagagag aaagatgcta gctccgcaag ccggagaggg aacaccgcca cattgttaca 660
cggacacacc gccacgtgga cacatgacca gactcacatg tacagacaca cggagacatt 720
accacatgga gacaccgtca cacagtccca cggacacact ggcatagtca catggacgga 780
cacacagaca tatggagaaa tcacatggac acaccaccac actatcacag ggacacagac 840
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gaagggaaga ggcctggggc tggagtattc gctt

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&lt;210&gt; 475

&lt;211&gt; 2414

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; unsure

&lt;222&gt; (33)

&lt;223&gt; n=A, T, C or G

&lt;400&gt; 475

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cccaacacaa tggctttata agaatgcttc acntgtgaaa aacaaatata aaagtcttct 60
tgtagattat ttttaaggac aaatctttat tccatgttta atttatttag ctttccctgt 120
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aaaaaaaaaa aaaa
2414

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&lt;210&gt; 476

&lt;211&gt; 3434

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 476

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ctgtgctgca aatggggcca tatagaggaa aggagcagct ggctctggag catggtgtgc 60
actccctttg ggccttcagt ccatgtctca tgggtcgtat gacactgcgg gcttgttgtt 120
tgccaagagg cagaccacag gtcactctga ggaggacttt atgttccagt ccagaaagca 180
gccagtggta ccacccaggg gacttgtgct tctgtggccc aggccagacg tagaatttga 240
caaagtcagg acggtctcag tcagagcagc atgtcgggtc ccggggcctg tgcattgcgg 300

```

```

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aaaaaaaaaa aaaa
3434

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&lt;210&gt; 477

&lt;211&gt; 140

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

165

&lt;400&gt; 477

```

Met Asp Gly His Thr Asp Ile Trp Arg Asn His Met Asp Thr Pro Pro
                    5              10              15
His Tyr His Arg Asp Thr Asp Thr Arg Arg His His His Met Asp Thr
                20              25              30
Leu Ser His Tyr His Arg Asp Thr Arg His His Thr Val Thr Trp Thr
                35              40              45
His His His Thr His Glu His Thr Asp Thr Leu Pro Tyr Gly His Trp
                50              55              60
His Thr His Cys His Thr Val Thr Trp Thr His Leu His Thr Ile Thr
                65              70              75              80
Pro Pro His Thr Leu Pro Val Asp Thr Arg Thr His Arg His Cys His
                85              90              95
Thr Asp Thr Gln Asn Thr Val Thr Arg Arg His His His Ala Asp Thr
                100              105              110
Pro Pro Leu Trp Cys Arg Leu Asn Tyr Pro Ala Gly Gly Thr Ala Val
                115              120              125
Ala Tyr Ser Cys Leu Ser Asp Trp Leu Ser Pro Gln
                130              135              140

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&lt;210&gt; 478

&lt;211&gt; 143

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 478

```

Met Tyr Arg His Thr Glu Thr Leu Pro His Gly Asp Thr Val Thr Gln
                    5              10              15
Ser His Gly His Thr Gly Ile Val Thr Trp Thr Asp Thr Gln Thr Tyr
                20              25              30
Gly Glu Ile Thr Trp Thr His His His Thr Ile Thr Gly Thr Gln Thr
                35              40              45
His Gly Asp Ile Thr Thr Trp Thr His Cys His Thr Thr Gly Thr
                50              55              60
Arg Asp Ile Thr Leu Ser His Gly His Thr Ile Thr His Met Asn Thr
                65              70              75              80
Pro Thr His Cys His Met Asp Thr Gly Thr His Thr Ala Thr Leu Ser
                85              90              95
His Gly His Thr Ser Thr Pro Ser His His His Thr His Cys Leu Trp
                100              105              110
Thr Gln Gly His Thr Asp Thr Val Thr Gln Ile His Lys Thr Leu Ser
                115              120              125
His Gly Asp Ile Thr Met Gln Ile His His His Ser Gly Ala Val
                130              135              140

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&lt;210&gt; 479

&lt;211&gt; 222

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 479

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Met Tyr Arg His Thr Glu Thr Leu Pro His Gly Asp Thr Val Thr Gln
                    5              10              15
Ser His Glu His Thr Gly Ile Val Thr Trp Thr Asp Thr Gln Thr Tyr
                20              25              30

```

166

Gly Glu Ile Thr Leu Thr His His His Thr Ile Thr Gly Thr Gln Thr  
           35                  40                  45  
 His Gly Asp Ile Thr Thr Trp Thr His Cys His Thr Thr Thr Gly Thr  
           50                  55                  60  
 Arg Asp Ile Thr Leu Ser His Gly His Thr Ile Thr His Met Asn Thr  
           65                  70                  75                  80  
 Pro Thr His Cys His Met Asp Thr Ala Thr His Thr Ala Thr Leu Ser  
                   85                  90                  95  
 His Gly His Thr Ser Ile Pro Ser His His His Thr His Cys His Val  
                  100                 105                 110  
 Asp Thr Arg Thr His Arg His Cys His Thr Asp Thr Gln Asn Thr Val  
                  115                 120                 125  
 Thr Arg Arg His His His Ala Asp Thr Pro Pro His Gly His Ser Thr  
                  130                 135                 140  
 Arg His Ser Ala Thr Gln Ile His His His Thr Glu Met Arg Thr His  
                  145                 150                 155                 160  
 Cys His Thr Asp Thr Thr Thr Ser Leu Pro His Phe His Val Ser Ala  
                  165                 170                 175  
 Gly Gly Val Gly Pro Thr Thr Leu Gly Ser Asn Arg Glu Ile Thr Trp  
                  180                 185                 190  
 Thr Tyr Ser Glu Gly Lys Ile Phe Phe Tyr Phe Leu Gly Asn Gln Ala  
                  195                 200                 205  
 Arg Leu Cys Leu Lys Lys Arg Lys Lys Lys Gln Tyr Thr Val  
                  210                 215                 220

&lt;210&gt; 480

&lt;211&gt; 144

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 480

Met Glu Pro Tyr Arg Gly Asn Glu Gln Pro Ser Gln Glu Gln Gly Val  
                   5                 10                 15  
 Cys Cys Leu Trp Gly Leu Gln Ser Leu Pro Gln Gly Ser Tyr Val Thr  
                  20                 25                 30  
 Val Gly Phe Leu Val Val Lys Arg Gln Thr Ile Gly Arg Leu Glu Arg  
                  35                 40                 45  
 Asp Phe Met Phe Lys Cys Arg Lys Gln Pro Gly Leu Pro Pro Ser Gly  
                  50                 55                 60  
 Leu Cys Leu Leu Trp Pro Trp Pro Asn Leu Glu Phe Gly Arg Arg Gln  
                  65                 70                 75                 80  
 Asp Arg Leu Thr Trp Ser Ser Val Ser Val Ala Gly Val Cys Ala Cys  
                  85                 90                 95  
 Arg Ala Arg Pro Gly Trp Leu Gly Glu Gln Pro Ala Thr Ser Ala Gly  
                  100                 105                 110  
 Val Arg Leu Glu Gln Val Glu Gln Pro Pro Ala His Pro Leu Gln Glu  
                  115                 120                 125  
 Ala Gly Val Ala Arg Phe Pro Arg Pro Glu Trp Val Pro Pro Asn Gly  
                  130                 135                 140

&lt;210&gt; 481

&lt;211&gt; 167

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 481

167

```

Met His Gly Pro Gln Val Leu Ala Arg Cys Ser Glu Cys Ala Cys Pro
      5              10              15
Ala Leu Ala Ala Thr Ser Ala Gly Val Arg Leu Glu Gly Val Asp Arg
      20              25              30
Pro Pro Thr Leu Pro Ser Gln Gly Ser Gly Trp Pro Cys Ser His Ser
      35              40              45
Leu Ser Gly Cys His Leu Met Ala Asp Gly Ala Lys Ala Leu Gly Lys
      50              55              60
Ala Asp Gly Pro Trp Pro Tyr Leu Phe Val Arg Arg Thr Asp Val Pro
      65              70              75              80
Cys Pro Ala Ala Ser Glu Val Gly Gly Cys Ala Pro Ser Ser Trp Arg
      85              90              95
Ala Leu Ala Glu Val Thr Gly Cys Ser Leu Gly Pro Leu Gly Leu Ala
      100             105             110
Gln His Ala Gln Ala Ser Val Leu Leu Cys Tyr Lys Trp Ser His
      115             120             125
Ile Gly Glu Thr Ser Ser His Leu Arg Ser Lys Val Tyr Ala Ala Phe
      130             135             140
Gly Gly Ser Ser Pro Cys Leu Lys Gly Leu Met Ser Leu Trp Ala Ser
      145             150             155             160
Trp Leu Ser Arg Gly Arg Pro
      165

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&lt;210&gt; 482

&lt;211&gt; 143

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 482

```

Met Glu Pro Tyr Arg Gly Asn Lys Lys Gln Val Gln Glu Lys Gly Val
      5              10              15
Pro Cys Leu Trp Gly Ser Ser Pro Cys Leu Arg Cys His Met Ala Leu
      20              25              30
Arg Ala Ser Trp Leu Pro Gly Gly Gly Pro Gln Ala Ile Leu Gly Arg
      35              40              45
Thr Leu Cys Ser Ser Ala Glu Ser Ser Gln Asp Cys His Pro Gly Gly
      50              55              60
Pro Ser Ile Ala Leu Ala Lys Pro Cys Arg Gly Val Trp Leu Leu Phe
      65              70              75              80
Glu Pro Ala Trp Pro Pro Trp His Ala Arg Ala Pro Gly Ala Gly Thr
      85              90              95
Leu Leu Arg Val Cys Leu Ser Cys Leu Gly Cys His Leu Cys Gly Gly
      100             105             110
Ala Ser Gly Gly Gly Gly Pro Ala Thr Asn Leu Thr Gln Ser Arg Lys
      115             120             125
Trp Met Ala Met Phe Pro Gln Pro Glu Trp Leu Pro Pro Asp Gly
      130             135             140

```

&lt;210&gt; 483

&lt;211&gt; 143

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 483

```

Met Glu Thr Gln Arg Gly Asn Lys Gln Arg Ala Gln Glu Gln Gly Val
      5              10              15
Cys Cys Leu Trp Gly Ser Ser Pro Cys Leu Gly Ser Tyr Gly Thr Ala

```



168

20 25 30  
 Gly Phe Leu Val Ala Lys Arg Arg Thr Thr Gly Leu Leu Glu Glu Asp  
 35 40 45  
 Phe Thr Phe Lys Cys Arg Lys Gln Pro Lys Leu Pro Ser Met Arg Leu  
 50 55 60  
 Ser Leu Leu Trp Pro Trp Arg Asp Leu Lys Phe Val Pro Arg Gln Asp  
 65 70 75 80  
 Lys Leu Thr Arg Ser Ser Val Ser Val Ala Gly Ala Tyr Ala Cys Arg  
 85 90 95  
 Ala Gly Pro Gly Trp Leu Lys Glu Gln Pro Ala Thr Ser Ala Arg Val  
 100 105 110  
 Arg Leu Val Gln Ala Glu His Pro Pro Pro His Pro Leu Glu Glu Val  
 115 120 125  
 Gly Met Ala Arg Phe Pro Gln Pro Glu Cys Leu Pro Pro Tyr Cys  
 130 135 140

<210> 484  
 <211> 30  
 <212> PRT  
 <213> Homo Sapien

<400> 484  
 Thr Ala Ala Ser Asp Asn Phe Gln Leu Ser Gln Gly Gly Gln Gly Phe  
 1 5 10 15  
 Ala Ile Pro Ile Gly Gln Ala Met Ala Ile Ala Gly Gln Ile  
 20 25 30

<210> 485  
 <211> 31  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 485  
 gggaagctta tcacctatgt gccgcctctg c

31

<210> 486  
 <211> 27  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 486  
 gcgaattctc acgctgagta tttaggcc

27

<210> 487  
 <211> 36  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 487

169

cccgaattct tagctgccca tccgaacgcc ttcac

36

<210> 488  
 <211> 33  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 488  
 gggaagcttc ttccccggct gcaccagctg tgc

33

<210> 489  
 <211> 19  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 489  
 Met Asp Arg Leu Val Gln Arg Phe Gly Thr Arg Ala Val Tyr Leu Ala  
 1 5 10 15  
 Ser Val Ala

<210> 490  
 <211> 20  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 490  
 Tyr Leu Ala Ser Val Ala Ala Phe Pro Val Ala Ala Gly Ala Thr Cys  
 1 5 10 15  
 Leu Ser His Ser  
 20

<210> 491  
 <211> 20  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 491  
 Thr Cys Leu Ser His Ser Val Ala Val Thr Ala Ser Ala Ala Leu  
 1 5 10 15  
 Thr Gly Phe Thr  
 20

<210> 492  
 <211> 20  
 <212> PRT

170

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 492

Ala	Leu	Thr	Gly	Phe	Thr	Phe	Ser	Ala	Leu	Gln	Ile	Leu	Pro	Tyr	Thr
1				5					10					15	
Leu	Ala	Ser	Leu												
				20											

&lt;210&gt; 493

&lt;211&gt; 20

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 493

Tyr	Thr	Leu	Ala	Ser	Leu	Tyr	His	Arg	Glu	Lys	Gln	Val	Phe	Leu	Pro
1				5					10					15	
Lys	Tyr	Arg	Gly												
				20											

&lt;210&gt; 494

&lt;211&gt; 20

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 494

Leu	Pro	Lys	Tyr	Arg	Gly	Asp	Thr	Gly	Gly	Ala	Ser	Ser	Glu	Asp	Ser
1				5					10					15	
Leu	Met	Ile	Ser												
				20											

&lt;210&gt; 495

&lt;211&gt; 20

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 495

Asp	Ser	Leu	Met	Thr	Ser	Phe	Leu	Pro	Gly	Pro	Lys	Pro	Gly	Ala	Pro
1				5					10					15	
Phe	Pro	Asn	Gly												
				20											

&lt;210&gt; 496

&lt;211&gt; 21

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

171

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 496

Ala	Pro	Phe	Pro	Asn	Gly	His	Val	Gly	Ala	Gly	Gly	Ser	Gly	Leu	Leu
1				5				10						15	
Pro	Pro	Pro	Pro	Ala											
				20											

&lt;210&gt; 497

&lt;211&gt; 20

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 497

Leu	Leu	Pro	Pro	Pro	Ala	Leu	Cys	Gly	Ala	Ser	Ala	Cys	Asp	Val
1				5				10					15	
Ser	Val	Arg	Val											
				20										

&lt;210&gt; 498

&lt;211&gt; 20

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 498

Asp	Val	Ser	Val	Arg	Val	Val	Val	Gly	Glu	Pro	Thr	Glu	Ala	Arg	Val
1				5				10						15	
Val	Pro	Gly	Arg												
				20											

&lt;210&gt; 499

&lt;211&gt; 20

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 499

Arg	Val	Val	Pro	Gly	Arg	Gly	Ile	Cys	Leu	Asp	Leu	Ala	Ile	Leu	Asp
1				5				10						15	
Ser	Ala	Phe	Leu												
				20											

&lt;210&gt; 500

&lt;211&gt; 20

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

172

&lt;223&gt; Made in a lab

&lt;400&gt; 500

Leu Asp Ser Ala Phe Leu Leu Ser Gln Val Ala Pro Ser Leu Phe Met  
 1 5 10 15  
 Gly Ser Ile Val  
 20

&lt;210&gt; 501

&lt;211&gt; 20

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 501

Phe Met Gly Ser Ile Val Gln Leu Ser Gln Ser Val Thr Ala Tyr Met  
 1 5 10 15  
 Val Ser Ala Ala  
 20

&lt;210&gt; 502

&lt;211&gt; 414

&lt;212&gt; DNA

&lt;213&gt; Homo Sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(414)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 502

caccatggag	acaggcctgc	gctggctttt	cctggctcgt	gtgctcaaag	gtgtccaatg	60
tcagtcggtg	gaggagtccg	ggggtcgcct	ggtcacgcct	gggacacctt	tgacantcac	120
ctgtagagtt	tttggaaatng	acctcagtag	caatgcaatg	agctgggtcc	gccaggctcc	180
aggggaagggg	ctggaatgga	tcggagccat	tgataattgt	ccacantacg	cgacctgggc	240
gaaaggccga	tttnatnattt	cctttttttt	gaccacgggtg	gatttgaaaa	tgaccagtcc	300
gacaaccgag	gacacggcca	cctatttttg	tggcagaatg	aatactggta	atagtgggtg	360
gaagaatatt	tggggcccag	gcaccctggg	caccgtntcc	tcagggcaac	ctaa	414

&lt;210&gt; 503

&lt;211&gt; 379

&lt;212&gt; DNA

&lt;213&gt; Homo Sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(379)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 503

atnccgatggt	gcttgggtcaa	agggtgtccag	tgtagtcggt	tgaggaggatc	cggggggtcgc	60
ctgggtcacgc	ctggggacacc	cctgacactc	acctgcaccg	tntctggatt	ngacatcagt	120
agctatggag	tgagctgggt	ccgccaggct	ccagggaagg	ggctggnata	catcggtatca	180
ttagtagtag	tggtacattt	tacgcgagct	gggcgaaaag	ccgattcacc	atttccaaaa	240
cctngaccac	ggtggatttg	aaaatcacca	gtttgacaac	cgaggacacg	gccacctatt	300
tntgtgccag	agggggggtt	aattataaag	acatttgggg	cccaggcacc	ctggtcaccg	360

173

tntccttagg gcaacctaa

379

<210> 504  
 <211> 19  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 504  
 Gly Phe Thr Asn Tyr Thr Asp Phe Glu Asp Ser Pro Tyr Phe Lys Glu  
 1 5 10 15  
 Asn Ser Ala

<210> 505  
 <211> 20  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 505  
 Lys Glu Asn Ser Ala Phe Pro Pro Phe Cys Cys Asn Asp Asn Val Thr  
 1 5 10 15  
 Asn Thr Ala Asn  
 20

<210> 506  
 <211> 407  
 <212> DNA  
 <213> Homo Sapien

<400> 506  
 atggagacag gcttgcgctg gcttctcctg gtcgctgctc tcaaagggtgt ccagtgtcag 60  
 tcgctggagg agtccggggg tcgcctgggc acgcctggga caccctgac actcacctgc 120  
 accgtctctg gattctccct cagtagcaat gcaatgatct gggcccgcca ggctccaggg 180  
 aaggggctgg aatacatcgg atacattagt tatgggtgta gcgcatacta cgcgagctgg 240  
 gtgaaaggcc gattcaccat ctccaaaacc tcgaccacgg tggatctgag aatgaccagt 300  
 ctgacaaccg aggacacggc cacctatttc tgtgccagaa atagtgattt tagtggtatg 360  
 ttgtggggcc caggcaccct ggtcaccgtc tcctcagggc aacctaa 407

<210> 507  
 <211> 422  
 <212> DNA  
 <213> Homo Sapien

<400> 507  
 atggagacag gcttgcgctg gcttctcctg gtcgctgtgc tcaaagggtgt ccagtgtcag 60  
 tcggtggagg agtccggggg tcgcctgggc acgcctggga caccctgac actcacctgt 120  
 acagtctctg gattctccct cagcaactac gacctgaact gggcccgcca ggctccaggg 180  
 aaggggctgg aatggatcgg gatcattaat tatgttgta ggacggacta cgcgaactgg 240  
 gcaaaaggcc ggttcaccat ctccaaaacc tcgaccacgg tggatctcaa gatcgccagt 300  
 ccgacaaccg aggacacggc cacctatttc tgtgccagag ggtggaagtg cgatgagtct 360  
 ggtccgtgct tgccgcatctg gggcccaggc accctgggtc ccgtctcctt agggcaacct 420

174

aa

422

<210> 508  
 <211> 411  
 <212> DNA  
 <213> Homo Sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(411)  
 <223> n=A,T,C or G

<400> 508  
 atggagacag gcctcgctgg cttctcctgg tcgctgtgct caaagggtgc cagtgtcagt 60  
 cgggtggagga gtccgggggt cgcctgggtca cgcctgggac acccctgaca ctcacctgca 120  
 cagtctctgg aatcgacctc agtagctact gcatgagctg ggtccgccag gctccaggga 180  
 aggggctgga atggatcgga atcattggta ctctgggtga cacatactac gcgagggtgg 240  
 cgaaaggccg attcaccatc tccaaaacct cgaccacggt gcatntgaaa atcnccagtc 300  
 cgacaaccga ggcacacgcc acctatttct gtgccagaga tcttcgggat ggtagtagta 360  
 ctggttatta taaaatctgg ggcccaggca ccctgggtcac cgtctccttg g 411

<210> 509  
 <211> 15  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 509  
 Leu Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser  
 1 5 10 15

<210> 510  
 <211> 15  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 510  
 Pro Glu Tyr Asn Arg Pro Leu Leu Ala Asn Asp Leu Met Leu Ile  
 1 5 10 15

<210> 511  
 <211> 15  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 511

Tyr His Pro Ser Met Phe Cys Ala Gly Gly Gly Gln Asp Gln Lys  
 1 5 10 15

175

<210> 512  
 <211> 15  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 512  
 Asp Ser Gly Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu  
 1 5 10 15

<210> 513  
 <211> 15  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 513  
 Ala Pro Cys Gly Gln Val Gly Val Pro Asx Val Tyr Thr Asn Leu  
 1 5 10 15

<210> 514  
 <211> 15  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 514  
 Leu Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser  
 1 5 10 15

<210> 515  
 <211> 15  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 515  
 Met Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg  
 1 5 10 15

<210> 516  
 <211> 15  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 516  
 Val Ser Glu Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln



176

1 5 10 15

<210> 517  
 <211> 15  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 517  
 Glu Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met  
 1 5 10 15

<210> 518  
 <211> 15  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 518  
 Arg Ala Glu Pro Gly Thr Glu Ala Arg Arg His Tyr Asp Glu Gly  
 1 5 10 15

<210> 519  
 <211> 17  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 519  
 Arg Ala Glu Pro Gly Thr Glu Ala Arg Arg Asn Tyr Asp Glu Gly Cys  
 1 5 10 15  
 Gly

<210> 520  
 <211> 25  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 520  
 Val Gly Glu Gly Leu Tyr Gln Gly Val Pro Arg Ala Glu Pro Gly Thr  
 1 5 10 15  
 Glu Ala Arg Arg His Tyr Asp Glu Gly  
 20 25

<210> 521  
 <211> 21  
 <212> PRT  
 <213> Artificial Sequence

177

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 521

Ala	Pro	Phe	Pro	Asn	Gly	His	Val	Gly	Ala	Gly	Gly	Ser	Gly	Leu	Leu
1				5					10					15	
Pro	Pro	Pro	Pro	Ala											
				20											

&lt;210&gt; 522

&lt;211&gt; 20

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;400&gt; 522

Leu	Leu	Val	Val	Pro	Ala	Ile	Lys	Lys	Asp	Tyr	Gly	Ser	Gln	Glu	Asp
1				5					10					15	
Phe	Thr	Gln	Val												
			20												

&lt;210&gt; 523

&lt;211&gt; 254

&lt;212&gt; PRT

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; Made in a lab

&lt;220&gt;

&lt;221&gt; VARIANT

&lt;222&gt; (1)...(254)

&lt;223&gt; Xaa = any amino acid

&lt;400&gt; 523

Met	Ala	Thr	Ala	Gly	Asn	Pro	Trp	Gly	Trp	Phe	Leu	Gly	Tyr	Leu	Ile
1				5					10					15	
Leu	Gly	Val	Ala	Gly	Ser	Leu	Val	Ser	Gly	Ser	Cys	Ser	Gln	Ile	Ile
		20						25					30		
Asn	Gly	Glu	Asp	Cys	Ser	Pro	His	Ser	Gln	Pro	Trp	Gln	Ala	Ala	Leu
		35					40					45			
Val	Met	Glu	Asn	Glu	Leu	Phe	Cys	Ser	Gly	Val	Leu	Val	His	Pro	Gln
	50					55				60					
Trp	Val	Leu	Ser	Ala	Thr	His	Cys	Phe	Gln	Asn	Ser	Tyr	Thr	Ile	Gly
	65				70				75					80	
Leu	Gly	Leu	His	Ser	Leu	Glu	Ala	Asp	Gln	Glu	Pro	Gly	Ser	Gln	Met
			85						90					95	
Val	Glu	Ala	Ser	Leu	Ser	Val	Arg	His	Pro	Glu	Tyr	Asn	Arg	Pro	Leu
		100					105						110		
Leu	Ala	Asn	Asp	Leu	Met	Leu	Ile	Lys	Leu	Asp	Glu	Ser	Val	Ser	Glu
	115					120					125				
Ser	Asp	Thr	Ile	Arg	Ser	Ile	Ser	Ile	Ala	Ser	Gln	Cys	Pro	Thr	Ala
	130					135				140					
Gly	Asn	Ser	Cys	Leu	Val	Ser	Gly	Trp	Gly	Leu	Leu	Ala	Asn	Gly	Arg
145					150					155					160

178

Met Pro Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu Glu  
 165 170 175  
 Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys  
 180 185 190  
 Ala Gly Gly Gly Gln Xaa Gln Xaa Asp Ser Cys Asn Gly Asp Ser Gly  
 195 200 205  
 Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly  
 210 215 220  
 Lys Ala Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn Leu  
 225 230 235 240  
 Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser  
 245 250

&lt;210&gt; 524

&lt;211&gt; 765

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 524

atggccacag	caggaaatcc	ctggggetgg	tctctggggt	acctcatcct	tggtgtcgca	60
ggatcgctcg	tctctggtag	ctgcagccaa	atcataaacg	gcgaggactg	cagcccgcac	120
tgcagccct	ggcaggcggc	actggtcatg	gaaaacgaat	tggtctgctc	ggcgctcctg	180
gtgcattccg	agtggtgct	gtcagccgca	cactgtttcc	agaactccta	caccatcggg	240
ctgggcctgc	acagtcttga	ggccgaccaa	gagccaggga	gccagatggt	ggaggccagc	300
ctctccgtac	ggcaccacaga	gtacaacaga	cccttgctcg	ctaacgacct	catgctcatc	360
aagttggacg	aatccgtgtc	cgagtctgac	accatccgga	gcattcagcat	tgcttcgcag	420
tgccctaccg	cggggaactc	ttgcctcgtt	tctggctggg	gtctgctggc	gaacggcaga	480
atgcctaccg	tgctgcagtg	cgtgaacgtg	tgggtggtgt	ctgaggaggt	ctgcagtaag	540
ctctatgacc	cgctgtacca	ccccagcatg	ttctgcgccg	gcggagggca	agaccagaag	600
gactcctgca	acggtgactc	tggggggccc	ctgatctgca	acgggtactt	gcagggcctt	660
gtgtctttcg	gaaaagcccc	gtgtggccaa	gttggcgtgc	cagggtgtcta	caccaacctc	720
tgcaaattca	ctgagtggat	agagaaaacc	gtccaggcca	gttaa		765

&lt;210&gt; 525

&lt;211&gt; 254

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 525

Met	Ala	Thr	Ala	Gly	Asn	Pro	Trp	Gly	Trp	Phe	Leu	Gly	Tyr	Leu	Ile
1				5				10					15		
Leu	Gly	Val	Ala	Gly	Ser	Leu	Val	Ser	Gly	Ser	Cys	Ser	Gln	Ile	Ile
			20					25					30		
Asn	Gly	Glu	Asp	Cys	Ser	Pro	His	Ser	Gln	Pro	Trp	Gln	Ala	Ala	Leu
		35					40					45			
Val	Met	Glu	Asn	Glu	Leu	Phe	Cys	Ser	Gly	Val	Leu	Val	His	Pro	Gln
		50				55					60				
Trp	Val	Leu	Ser	Ala	Ala	His	Cys	Phe	Gln	Asn	Ser	Tyr	Thr	Ile	Gly
65				70					75					80	
Leu	Gly	Leu	His	Ser	Leu	Glu	Ala	Asp	Gln	Glu	Pro	Gly	Ser	Gln	Met
			85					90						95	
Val	Glu	Ala	Ser	Leu	Ser	Val	Arg	His	Pro	Glu	Tyr	Asn	Arg	Pro	Leu
			100					105				110			
Leu	Ala	Asn	Asp	Leu	Met	Leu	Ile	Lys	Leu	Asp	Glu	Ser	Val	Ser	Glu
		115					120					125			
Ser	Asp	Thr	Ile	Arg	Ser	Ile	Ser	Ile	Ala	Ser	Gln	Cys	Pro	Thr	Ala
		130				135					140				
Gly	Asn	Ser	Cys	Leu	Val	Ser	Gly	Trp	Gly	Leu	Leu	Ala	Asn	Gly	Arg

179

145                      150                      155                      160  
 Met Pro Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu Glu  
                                  165                      170                      175  
 Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys  
                                  180                      185                      190  
 Ala Gly Gly Gly Gln Asp Gln Lys Asp Ser Cys Asn Gly Asp Ser Gly  
                                  195                      200                      205  
 Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly  
                                  210                      215                      220  
 Lys Ala Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn Leu  
 225                      230                      235                      240  
 Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser  
                                  245                      250

&lt;210&gt; 526

&lt;211&gt; 963

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 526

atgagttcct gcaacttcac acatgccacc tttgtgctta ttggtatccc aggattagag 60  
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 aactgcatcg tggctcttcat cgttaaggacg gaacgcagcc tgcacgctcc gatgtacctc 180  
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&lt;210&gt; 527

&lt;211&gt; 320

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 527

Met Ser Ser Cys Asn Phe Thr His Ala Thr Phe Val Leu Ile Gly Ile  
                                  5                      10                      15  
 Pro Gly Leu Glu Lys Ala His Phe Trp Val Gly Phe Pro Leu Leu Ser  
                                  20                      25                      30  
 Met Tyr Val Val Ala Met Phe Gly Asn Cys Ile Val Val Phe Ile Val  
                                  35                      40                      45  
 Arg Thr Glu Arg Ser Leu His Ala Pro Met Tyr Leu Phe Leu Cys Met  
                                  50                      55                      60  
 Leu Ala Ala Ile Asp Leu Ala Leu Ser Thr Ser Thr Met Pro Lys Ile  
                                  65                      70                      75                      80  
 Leu Ala Leu Phe Trp Phe Asp Ser Arg Glu Ile Ser Phe Glu Ala Cys  
                                  85                      90                      95  
 Leu Thr Gln Met Phe Phe Ile His Ala Leu Ser Ala Ile Glu Ser Thr  
                                  100                      105                      110

180

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Ile Leu Leu Ala Met Ala Phe Asp Arg Tyr Val Ala Ile Cys His Pro
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Leu Arg His Ala Ala Val Leu Asn Asn Thr Val Thr Ala Gln Ile Gly
    130                135                140
Ile Val Ala Val Val Arg Gly Ser Leu Phe Phe Phe Pro Leu Pro Leu
    145                150                155                160
Leu Ile Lys Arg Leu Ala Phe Cys His Ser Asn Val Leu Ser His Ser
    165                170                175
Tyr Cys Val His Gln Asp Val Met Lys Leu Ala Tyr Ala Asp Thr Leu
    180                185                190
Pro Asn Val Val Tyr Gly Leu Thr Ala Ile Leu Leu Val Met Gly Val
    195                200                205
Asp Val Met Phe Ile Ser Leu Ser Tyr Phe Leu Ile Ile Arg Thr Val
    210                215                220
Leu Gln Leu Pro Ser Lys Ser Glu Arg Ala Lys Ala Phe Gly Thr Cys
    225                230                235                240
Val Ser His Ile Gly Val Val Leu Ala Phe Tyr Val Pro Leu Ile Gly
    245                250                255
Leu Ser Val Val His Arg Phe Gly Asn Ser Leu His Pro Ile Val Arg
    260                265                270
Val Val Met Gly Asp Ile Tyr Leu Leu Leu Pro Pro Val Ile Asn Pro
    275                280                285
Ile Ile Tyr Gly Ala Lys Thr Lys Gln Ile Arg Thr Arg Val Leu Ala
    290                295                300
Met Phe Lys Ile Ser Cys Asp Lys Asp Leu Gln Ala Val Gly Gly Lys
    305                310                315                320

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 <213> Homo Sapien

<400> 528  
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20

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20

<210> 530  
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&lt;210&gt; 531

&lt;211&gt; 879

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 531

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cggccagaga gtatgctgtt tctagtcatc atcatgtaa 879

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&lt;210&gt; 532

&lt;211&gt; 292

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 532

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Met His Leu Ser Phe Pro Ala Phe Leu Pro Pro Trp Met Asp Arg Gly
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Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp His Asn Asp Ser Ser
      20              25              30
Val Lys Thr Leu Gly Ser Lys Arg Cys Lys Trp Cys Cys His Cys Phe
      35              40              45
Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val Val Ala Trp Gly Asp

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182

50	55	60
Tyr Asp Asp Ser Ala Phe Met Asp Pro Arg Tyr His Val His Gly Glu		
65	70	75
Asp Leu Asp Lys Leu His Arg Ala Ala Trp Trp Gly Lys Val Pro Arg		80
	85	90
Lys Asp Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys Arg Asp		95
	100	105
Lys Gln Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly Asn Ser		110
	115	120
Glu Val Val Lys Leu Val Leu Asp Arg Arg Cys Gln Leu Asn Val Leu		125
	130	135
Asp Asn Lys Lys Arg Thr Ala Leu Thr Lys Ala Val Gln Cys Gln Glu		140
	145	150
Asp Glu Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro Asn Ile		155
	165	170
Pro Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Val Tyr Asn Glu		175
	180	185
Asp Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu		190
	195	200
Ser Lys Asn Lys His Gly Leu Thr Pro Leu Leu Leu Gly Ile His Glu		205
	210	215
Gln Lys Gln Gln Val Val Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu		220
	225	230
Asn Ala Leu Asp Arg Tyr Gly Arg Thr Ala Leu Ile Leu Ala Val Cys		235
	245	250
Cys Gly Ser Ala Ser Ile Val Ser Pro Leu Leu Glu Gln Asn Val Asp		255
	260	265
Val Ser Ser Gln Asp Leu Glu Arg Arg Pro Glu Ser Met Leu Phe Leu		270
	275	280
Val Ile Ile Met		285
290		

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<210> 534  
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 <212> PRT  
 <213> Homo sapiens

183

&lt;400&gt; 534

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Arg Lys Gln Ala Ala Gly Ser Gly Ala Gly Tyr Ala Leu Pro Ser Ala
      20      25      30
Leu Gln Ser Met Pro Gln Gly Ser Tyr Ala Thr Ala Arg Phe Leu Val
      35      40      45
Ala Lys Arg Pro Thr Thr Gly His Leu Glu Lys Glu Phe Met Phe His
      50      55      60
Cys Arg Lys Gln Pro Gly Ser Pro Ser Arg Gly Leu Gly Leu Leu Trp
      65      70      75      80
Pro Trp Pro Asp Ile Glu Phe Val Pro Arg Gln Asp Lys Leu Thr Gln
      85      90      95
Ser Ser Val Leu Val Pro Gln Ile Cys Ala Cys Gln Thr Arg Pro Asn
      100      105      110
Trp Leu Asn Glu Gln Pro Ala Thr Ser Ala Gly Val Arg Leu Glu Glu
      115      120      125
Val Asp Gln Pro Pro Thr Leu Pro Ser Gln Gly Ser Gly Trp Pro Cys
      130      135      140
Ser His Ser Leu Ser Gly Cys His Leu Met Ala Asp Ile Ala Lys Ala
      145      150      155      160
Leu Gly Lys Ala Asp Gly Pro Trp Pro Tyr Leu Phe Val Arg Arg Thr
      165      170      175
Asp Val Pro Cys Pro Ala Ala Ser Glu Val Gly Gly Cys Ala Pro Ser
      180      185      190
Ser Trp His Thr Leu Ala Glu Val Thr Gly Cys Ser Leu Ser Pro Leu
      195      200      205
Ser Leu Ala Gln His Ala Gln Ala Ser Val Leu Leu Cys Tyr Lys
      210      215      220
Trp Ser His Ile Gly Glu Thr Ser Ser His Leu Arg Ser Lys Val Tyr
      225      230      235      240
Ala Ala Phe Gly Gly Ser Ser Pro Cys Leu Lys Gly Leu Met Ser Leu
      245      250      255
Trp Ala Ser Trp Leu Pro Arg Gly Arg Pro
      260      265

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&lt;210&gt; 535

&lt;211&gt; 6082

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 535

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&lt;210&gt; 536

&lt;211&gt; 6140

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)... (6140)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 536

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&lt;210&gt; 537

&lt;211&gt; 1228

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 537

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Met Leu Pro Val Tyr Gln Glu Val Lys Pro Asn Pro Leu Gln Asp Ala
      5              10              15
Asn Leu Cys Ser Arg Val Phe Phe Trp Trp Leu Asn Pro Leu Phe Lys
      20              25              30
Ile Gly His Lys Arg Arg Leu Glu Glu Asp Asp Met Tyr Ser Val Leu
      35              40              45
Pro Glu Asp Arg Ser Gln His Leu Gly Glu Glu Leu Gln Gly Phe Trp
      50              55              60
Asp Lys Glu Val Leu Arg Ala Glu Asn Asp Ala Gln Lys Pro Ser Leu
      65              70              75              80
Thr Arg Ala Ile Ile Lys Cys Tyr Trp Lys Ser Tyr Leu Val Leu Gly
      85              90              95
Ile Phe Thr Leu Ile Glu Glu Ser Ala Lys Val Ile Gln Pro Ile Phe
      100             105             110
Leu Gly Lys Ile Ile Asn Tyr Phe Glu Asn Tyr Asp Pro Met Asp Ser
      115             120             125
Val Ala Leu Asn Thr Ala Tyr Ala Tyr Ala Thr Val Leu Thr Phe Cys
      130             135             140
Thr Leu Ile Leu Ala Ile Leu His His Leu Tyr Phe Tyr His Val Gln
      145             150             155             160
Cys Ala Gly Met Arg Leu Arg Val Ala Met Cys His Met Ile Tyr Arg
      165             170             175

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188

Lys Ala Leu Arg Leu Ser Asn Met Ala Met Gly Lys Thr Thr Thr Gly  
 180 185 190  
 Gln Ile Val Asn Leu Leu Ser Asn Asp Val Asn Lys Phe Asp Gln Val  
 195 200 205  
 Thr Val Phe Leu His Phe Leu Trp Ala Gly Pro Leu Gln Ala Ile Ala  
 210 215 220  
 Val Thr Ala Leu Leu Trp Met Glu Ile Gly Ile Ser Cys Leu Ala Gly  
 225 230 235 240  
 Met Ala Val Leu Ile Ile Leu Leu Pro Leu Gln Ser Cys Phe Gly Lys  
 245 250 255  
 Leu Phe Ser Ser Leu Arg Ser Lys Thr Ala Thr Phe Thr Asp Ala Arg  
 260 265 270  
 Ile Arg Thr Met Asn Glu Val Ile Thr Gly Ile Arg Ile Ile Lys Met  
 275 280 285  
 Tyr Ala Trp Glu Lys Ser Phe Ser Asn Leu Ile Thr Asn Leu Arg Lys  
 290 295 300  
 Lys Glu Ile Ser Lys Ile Leu Arg Ser Ser Cys Leu Arg Gly Met Asn  
 305 310 315 320  
 Leu Ala Ser Phe Phe Ser Ala Ser Lys Ile Ile Val Phe Val Thr Phe  
 325 330 335  
 Thr Thr Tyr Val Leu Leu Gly Ser Val Ile Thr Ala Ser Arg Val Phe  
 340 345 350  
 Val Ala Val Thr Leu Tyr Gly Ala Val Arg Leu Thr Val Thr Leu Phe  
 355 360 365  
 Phe Pro Ser Ala Ile Glu Arg Val Ser Glu Ala Ile Val Ser Ile Arg  
 370 375 380  
 Arg Ile Gln Thr Phe Leu Leu Leu Asp Glu Ile Ser Gln Arg Asn Arg  
 385 390 395 400  
 Gln Leu Pro Ser Asp Gly Lys Lys Met Val His Val Gln Asp Phe Thr  
 405 410 415  
 Ala Phe Trp Asp Lys Ala Ser Glu Thr Pro Thr Leu Gln Gly Leu Ser  
 420 425 430  
 Phe Thr Val Arg Pro Gly Glu Leu Leu Ala Val Val Gly Pro Val Gly  
 435 440 445  
 Ala Gly Lys Ser Ser Leu Leu Ser Ala Val Leu Gly Glu Leu Ala Pro  
 450 455 460  
 Ser His Gly Leu Val Ser Val His Gly Arg Ile Ala Tyr Val Ser Gln  
 465 470 475 480  
 Gln Pro Trp Val Phe Ser Gly Thr Leu Arg Ser Asn Ile Leu Phe Gly  
 485 490 495  
 Lys Lys Tyr Glu Lys Glu Arg Tyr Glu Lys Val Ile Lys Ala Cys Ala  
 500 505 510  
 Leu Lys Lys Asp Leu Gln Leu Leu Glu Asp Gly Asp Leu Thr Val Ile  
 515 520 525  
 Gly Asp Arg Gly Thr Thr Leu Ser Gly Gly Gln Lys Ala Arg Val Asn  
 530 535 540  
 Leu Ala Arg Ala Val Tyr Gln Asp Ala Asp Ile Tyr Leu Leu Asp Asp  
 545 550 555 560  
 Pro Leu Ser Ala Val Asp Ala Glu Val Ser Arg His Leu Phe Glu Leu  
 565 570 575  
 Cys Ile Cys Gln Ile Leu His Glu Lys Ile Thr Ile Leu Val Thr His  
 580 585 590  
 Gln Leu Gln Tyr Leu Lys Ala Ala Ser Gln Ile Leu Ile Leu Lys Asp  
 595 600 605  
 Gly Lys Met Val Gln Lys Gly Thr Tyr Thr Glu Phe Leu Lys Ser Gly  
 610 615 620  
 Ile Asp Phe Gly Ser Leu Leu Lys Lys Asp Asn Glu Glu Ser Glu Gln  
 625 630 635 640

Pro Pro Val Pro Gly Thr Pro Thr Leu Arg Asn Arg Thr Phe Ser Glu  
 645 650 655  
 Ser Ser Val Trp Ser Gln Gln Ser Ser Arg Pro Ser Leu Lys Asp Gly  
 660 665 670  
 Ala Leu Glu Ser Gln Asp Thr Glu Asn Val Pro Val Thr Leu Ser Glu  
 675 680 685  
 Glu Asn Arg Ser Glu Gly Lys Val Gly Phe Gln Ala Tyr Lys Asn Tyr  
 690 695 700  
 Phe Arg Ala Gly Ala His Trp Ile Val Phe Ile Phe Leu Ile Leu Leu  
 705 710 715 720  
 Asn Thr Ala Ala Gln Val Ala Tyr Val Leu Gln Asp Trp Trp Leu Ser  
 725 730 735  
 Tyr Trp Ala Asn Lys Gln Ser Met Leu Asn Val Thr Val Asn Gly Gly  
 740 745 750  
 Gly Asn Val Thr Glu Lys Leu Asp Leu Asn Trp Tyr Leu Gly Ile Tyr  
 755 760 765  
 Ser Gly Leu Thr Val Ala Thr Val Leu Phe Gly Ile Ala Arg Ser Leu  
 770 775 780  
 Leu Val Phe Tyr Val Leu Val Asn Ser Ser Gln Thr Leu His Asn Lys  
 785 790 795 800  
 Met Phe Glu Ser Ile Leu Lys Ala Pro Val Leu Phe Phe Asp Arg Asn  
 805 810 815  
 Pro Ile Gly Arg Ile Leu Asn Arg Phe Ser Lys Asp Ile Gly His Leu  
 820 825 830  
 Asp Asp Leu Leu Pro Leu Thr Phe Leu Asp Phe Ile Gln Thr Leu Leu  
 835 840 845  
 Gln Val Val Gly Val Val Ser Val Ala Val Ala Val Ile Pro Trp Ile  
 850 855 860  
 Ala Ile Pro Leu Val Pro Leu Gly Ile Ile Phe Ile Phe Leu Arg Arg  
 865 870 875 880  
 Tyr Phe Leu Glu Thr Ser Arg Asp Val Lys Arg Leu Glu Ser Thr Thr  
 885 890 895  
 Arg Ser Pro Val Phe Ser His Leu Ser Ser Ser Leu Gln Gly Leu Trp  
 900 905 910  
 Thr Ile Arg Ala Tyr Lys Ala Glu Glu Arg Cys Gln Glu Leu Phe Asp  
 915 920 925  
 Ala His Gln Asp Leu His Ser Glu Ala Trp Phe Leu Phe Leu Thr Thr  
 930 935 940  
 Ser Arg Trp Phe Ala Val Arg Leu Asp Ala Ile Cys Ala Met Phe Val  
 945 950 955 960  
 Ile Ile Val Ala Phe Gly Ser Leu Ile Leu Ala Lys Thr Leu Asp Ala  
 965 970 975  
 Gly Gln Val Gly Leu Ala Leu Ser Tyr Ala Leu Thr Leu Met Gly Met  
 980 985 990  
 Phe Gln Trp Cys Val Arg Gln Ser Ala Glu Val Glu Asn Met Met Ile  
 995 1000 1005  
 Ser Val Glu Arg Val Ile Glu Tyr Thr Asp Leu Glu Lys Glu Ala Pro  
 1010 1015 1020  
 Trp Glu Tyr Gln Lys Arg Pro Pro Pro Ala Trp Pro His Glu Gly Val  
 1025 1030 1035 1040  
 Ile Ile Phe Asp Asn Val Asn Phe Met Tyr Ser Pro Gly Gly Pro Leu  
 1045 1050 1055  
 Val Leu Lys His Leu Thr Ala Leu Ile Lys Ser Gln Glu Lys Val Gly  
 1060 1065 1070  
 Ile Val Gly Arg Thr Gly Ala Gly Lys Ser Ser Leu Ile Ser Ala Leu  
 1075 1080 1085  
 Phe Arg Leu Ser Glu Pro Glu Gly Lys Ile Trp Ile Asp Lys Ile Leu  
 1090 1095 1100

190

Thr Thr Glu Ile Gly Leu His Asp Leu Arg Lys Lys Met Ser Ile Ile  
 1105 1110 1115 1120  
 Pro Gln Glu Pro Val Leu Phe Thr Gly Thr Met Arg Lys Asn Leu Asp  
 1125 1130 1135  
 Pro Phe Asn Glu His Thr Asp Glu Glu Leu Trp Asn Ala Leu Gln Glu  
 1140 1145 1150  
 Val Gln Leu Lys Glu Thr Ile Glu Asp Leu Pro Gly Lys Met Asp Thr  
 1155 1160 1165  
 Glu Leu Ala Glu Ser Gly Ser Asn Phe Ser Val Gly Gln Arg Gln Leu  
 1170 1175 1180  
 Val Cys Leu Ala Arg Ala Ile Leu Arg Lys Asn Gln Ile Leu Ile Ile  
 1185 1190 1195 1200  
 Asp Glu Ala Thr Ala Asn Val Asp Pro Arg Thr Asp Glu Leu Ile Gln  
 1205 1210 1215  
 Lys Lys Ser Gly Arg Asn Leu Pro Thr Ala Pro Cys  
 1220 1225

&lt;210&gt; 538

&lt;211&gt; 1261

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 538

Met Tyr Ser Val Leu Pro Glu Asp Arg Ser Gln His Leu Gly Glu Glu  
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 Leu Gln Gly Phe Trp Asp Lys Glu Val Leu Arg Ala Glu Asn Asp Ala  
 20 25 30  
 Gln Lys Pro Ser Leu Thr Arg Ala Ile Ile Lys Cys Tyr Trp Lys Ser  
 35 40 45  
 Tyr Leu Val Leu Gly Ile Phe Thr Leu Ile Glu Glu Ser Ala Lys Val  
 50 55 60  
 Ile Gln Pro Ile Phe Leu Gly Lys Ile Ile Asn Tyr Phe Glu Asn Tyr  
 65 70 75 80  
 Asp Pro Met Asp Ser Val Ala Leu Asn Thr Ala Tyr Ala Tyr Ala Thr  
 85 90 95  
 Val Leu Thr Phe Cys Thr Leu Ile Leu Ala Ile Leu His His Leu Tyr  
 100 105 110  
 Phe Tyr His Val Gln Cys Ala Gly Met Arg Leu Arg Val Ala Met Cys  
 115 120 125  
 His Met Ile Tyr Arg Lys Ala Leu Arg Leu Ser Asn Met Ala Met Gly  
 130 135 140  
 Lys Thr Thr Thr Gly Gln Ile Val Asn Leu Leu Ser Asn Asp Val Asn  
 145 150 155 160  
 Lys Phe Asp Gln Val Thr Val Phe Leu His Phe Leu Trp Ala Gly Pro  
 165 170 175  
 Leu Gln Ala Ile Ala Val Thr Ala Leu Leu Trp Met Glu Ile Gly Ile  
 180 185 190  
 Ser Cys Leu Ala Gly Met Ala Val Leu Ile Ile Leu Leu Pro Leu Gln  
 195 200 205  
 Ser Cys Phe Gly Lys Leu Phe Ser Ser Leu Arg Ser Lys Thr Ala Thr  
 210 215 220  
 Phe Thr Asp Ala Arg Ile Arg Thr Met Asn Glu Val Ile Thr Gly Ile  
 225 230 235 240  
 Arg Ile Ile Lys Met Tyr Ala Trp Glu Lys Ser Phe Ser Asn Leu Ile  
 245 250 255  
 Thr Asn Leu Arg Lys Lys Glu Ile Ser Lys Ile Leu Arg Ser Ser Cys  
 260 265 270  
 Leu Arg Gly Met Asn Leu Ala Ser Phe Phe Ser Ala Ser Lys Ile Ile

		275						280				285			
Val	Phe	Val	Thr	Phe	Thr	Thr	Tyr	Val	Leu	Leu	Gly	Ser	Val	Ile	Thr
	290						295				300				
Ala	Ser	Arg	Val	Phe	Val	Ala	Val	Thr	Leu	Tyr	Gly	Ala	Val	Arg	Leu
305					310						315				320
Thr	Val	Thr	Leu	Phe	Phe	Pro	Ser	Ala	Ile	Glu	Arg	Val	Ser	Glu	Ala
				325						330					335
Ile	Val	Ser	Ile	Arg	Arg	Ile	Gln	Thr	Phe	Leu	Leu	Leu	Asp	Glu	Ile
			340					345					350		
Ser	Gln	Arg	Asn	Arg	Gln	Leu	Pro	Ser	Asp	Gly	Lys	Lys	Met	Val	His
		355					360					365			
Val	Gln	Asp	Phe	Thr	Ala	Phe	Trp	Asp	Lys	Ala	Ser	Glu	Thr	Pro	Thr
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Leu	Gln	Gly	Leu	Ser	Phe	Thr	Val	Arg	Pro	Gly	Glu	Leu	Leu	Ala	Val
385					390					395					400
Val	Gly	Pro	Val	Gly	Ala	Gly	Lys	Ser	Ser	Leu	Leu	Ser	Ala	Val	Leu
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Gly	Glu	Leu	Ala	Pro	Ser	His	Gly	Leu	Val	Ser	Val	His	Gly	Arg	Ile
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Ala	Tyr	Val	Ser	Gln	Gln	Pro	Trp	Val	Phe	Ser	Gly	Thr	Leu	Arg	Ser
		435					440					445			
Asn	Ile	Leu	Phe	Gly	Lys	Lys	Tyr	Glu	Lys	Glu	Arg	Tyr	Glu	Lys	Val
	450					455					460				
Ile	Lys	Ala	Cys	Ala	Leu	Lys	Lys	Asp	Leu	Gln	Leu	Leu	Glu	Asp	Gly
465				470						475					480
Asp	Leu	Thr	Val	Ile	Gly	Asp	Arg	Gly	Thr	Thr	Leu	Ser	Gly	Gly	Gln
				485					490					495	
Lys	Ala	Arg	Val	Asn	Leu	Ala	Arg	Ala	Val	Tyr	Gln	Asp	Ala	Asp	Ile
			500					505					510		
Tyr	Leu	Leu	Asp	Asp	Pro	Leu	Ser	Ala	Val	Asp	Ala	Glu	Val	Ser	Arg
		515					520					525			
His	Leu	Phe	Glu	Leu	Cys	Ile	Cys	Gln	Ile	Leu	His	Glu	Lys	Ile	Thr
	530					535					540				
Ile	Leu	Val	Thr	His	Gln	Leu	Gln	Tyr	Leu	Lys	Ala	Ala	Ser	Gln	Ile
545					550					555					560
Leu	Ile	Leu	Lys	Asp	Gly	Lys	Met	Val	Gln	Lys	Gly	Thr	Tyr	Thr	Glu
				565					570					575	
Phe	Leu	Lys	Ser	Gly	Ile	Asp	Phe	Gly	Ser	Leu	Leu	Lys	Lys	Asp	Asn
			580					585					590		
Glu	Glu	Ser	Glu	Gln	Pro	Pro	Val	Pro	Gly	Thr	Pro	Thr	Leu	Arg	Asn
		595					600					605			
Arg	Thr	Phe	Ser	Glu	Ser	Ser	Val	Trp	Ser	Gln	Gln	Ser	Ser	Arg	Pro
	610					615						620			
Ser	Leu	Lys	Asp	Gly	Ala	Leu	Glu	Ser	Gln	Asp	Thr	Glu	Asn	Val	Pro
625															



				740						745				750		
Thr	Leu	His	Asn	Lys	Met	Phe	Glu	Ser	Ile	Leu	Lys	Ala	Pro	Val	Leu	
		755					760					765				
Phe	Phe	Asp	Arg	Asn	Pro	Ile	Gly	Arg	Ile	Leu	Asn	Arg	Phe	Ser	Lys	
	770					775					780					
Asp	Ile	Gly	His	Leu	Asp	Asp	Leu	Leu	Pro	Leu	Thr	Phe	Leu	Asp	Phe	
785					790					795					800	
Ile	Gln	Thr	Leu	Leu	Gln	Val	Val	Gly	Val	Val	Ser	Val	Ala	Val	Ala	
				805					810					815		
Val	Ile	Pro	Trp	Ile	Ala	Ile	Pro	Leu	Val	Pro	Leu	Gly	Ile	Ile	Phe	
			820					825					830			
Ile	Phe	Leu	Arg	Arg	Tyr	Phe	Leu	Glu	Thr	Ser	Arg	Asp	Val	Lys	Arg	
	835					840					845					
Leu	Glu	Ser	Thr	Thr	Arg	Ser	Pro	Val	Phe	Ser	His	Leu	Ser	Ser	Ser	
	850					855					860					
Leu	Gln	Gly	Leu	Trp	Thr	Ile	Arg	Ala	Tyr	Lys	Ala	Glu	Glu	Arg	Cys	
865					870					875					880	
Gln	Glu	Leu	Phe	Asp	Ala	His	Gln	Asp	Leu	His	Ser	Glu	Ala	Trp	Phe	
				885				890						895		
Leu	Phe	Leu	Thr	Thr	Ser	Arg	Trp	Phe	Ala	Val	Arg	Leu	Asp	Ala	Ile	
			900					905					910			
Cys	Ala	Met	Phe	Val	Ile	Ile	Val	Ala	Phe	Gly	Ser	Leu	Ile	Leu	Ala	
	915						920					925				
-Lys	Thr	Leu	Asp	Ala	Gly	Gln	Val	Gly	Leu	Ala	Leu	Ser	Tyr	Ala	Leu	
	930				935						940					
Thr	Leu	Met	Gly	Met	Phe	Gln	Trp	Cys	Val	Arg	Gln	Ser	Ala	Glu	Val	
945					950					955					960	
Glu	Asn	Met	Met	Ile	Ser	Val	Glu	Arg	Val	Ile	Glu	Tyr	Thr	Asp	Leu	
				965					970					975		
Glu	Lys	Glu	Ala	Pro	Trp	Glu	Tyr	Gln	Lys	Arg	Pro	Pro	Pro	Ala	Trp	
			980.					985				990				
Pro	His	Glu	Gly	Val	Ile	Ile	Phe	Asp	Asn	Val	Asn	Phe	Met	Tyr	Ser	
	995						1000					1005				
Pro	Gly	Gly	Pro	Leu	Val	Leu	Lys	His	Leu	Thr	Ala	Leu	Ile	Lys	Ser	
	1010					1015					1020					
Gln	Glu	Lys	Val	Gly	Ile	Val	Gly	Arg	Thr	Gly	Ala	Gly	Lys	Ser	Ser	
1025					1030					1035					1040	
Leu	Ile	Ser	Ala	Leu	Phe	Arg	Leu	Ser	Glu	Pro	Glu	Gly	Lys	Ile	Trp	
				1045					1050					1055		
Ile	Asp	Lys	Ile	Leu	Thr	Thr	Glu	Ile	Gly	Leu	His	Asp	Leu	Arg	Lys	
			1060					1065					1070			
Lys	Met	Ser	Ile	Ile	Pro	Gln	Glu	Pro	Val	Leu	Phe	Thr				

193

```

      1205      1210      1215
Val Leu Leu Gln Asn Lys Glu Ser Leu Phe Tyr Lys Met Val Gln Gln
      1220      1225      1230
Leu Gly Lys Ala Glu Ala Ala Ala Leu Thr Glu Thr Ala Lys Gln Arg
      1235      1240      1245
Trp Gly Phe Thr Met Leu Ala Arg Leu Val Ser Asn Ser
      1250      1255      1260

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<210> 539  
 <211> 10  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 539  
 Cys Leu Ser His Ser Val Ala Val Val Thr  
 1 5 10

<210> 540  
 <211> 9  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 540  
 Ala Val Val Thr Ala Ser Ala Ala Leu  
 1 5

<210> 541  
 <211> 14  
 <212> PRT  
 <213> Homo sapiens

<400> 541  
 Leu Ala Gly Leu Leu Cys Pro Asp Pro Arg Pro Leu Glu Leu  
 5 10

<210> 542  
 <211> 15  
 <212> PRT  
 <213> Homo sapiens

<400> 542  
 Thr Gln Val Val Phe Asp Lys Ser Asp Leu Ala Lys Tyr Ser Ala  
 5 10 15

<210> 543  
 <211> 12  
 <212> PRT  
 <213> Homo sapiens

<400> 543  
 Phe Met Gly Ser Ile Val Gln Leu Ser Gln Ser Val  
 5 10

194

<210> 544  
 <211> 18  
 <212> PRT  
 <213> Homo sapiens

<400> 544  
 Thr Tyr Val Pro Pro Leu Leu Leu Glu Val Gly Val Glu Glu Lys Phe  
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 Met Thr

<210> 545  
 <211> 18  
 <212> PRT  
 <213> Homo sapiens

<400> 545  
 Met Asp Arg Leu Val Gln Arg Phe Gly Thr Arg Ala Val Tyr Leu Ala  
                                   5                                  10                                  15  
 Ser Val

<210> 546  
 <211> 29  
 <212> PRT  
 <213> Homo sapiens

<400> 546  
 Phe Val Gly Glu Gly Leu Tyr Gln Gly Val Pro Arg Ala Glu Pro Gly  
                                   5                                  10                                  15  
 Thr Glu Ala Arg Arg His Tyr Asp Glu Gly Val Arg Met  
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<210> 547  
 <211> 58  
 <212> PRT  
 <213> Homo sapiens

<400> 547  
 Val Ala Glu Glu Ala Ala Leu Gly Pro Thr Glu Pro Ala Glu Gly Leu  
                                   5                                  10                                  15  
 Ser Ala Pro Ser Leu Ser Pro His Cys Cys Pro Cys Arg Ala Arg Leu  
                                   20                                  25                                  30  
 Ala Phe Arg Asn Leu Gly Ala Leu Leu Pro Arg Leu His Gln Leu Cys  
                                   35                                  40                                  45  
 Cys Arg Met Pro Arg Thr Leu Arg Arg Leu  
                                   50                                  55

<210> 548  
 <211> 18  
 <212> PRT  
 <213> Homo sapiens

<400> 548  
 Ile Asp Trp Asp Thr Ser Ala Leu Ala Pro Tyr Leu Gly Thr Gln Glu

195

Glu Cys 5 10 15

<210> 549  
 <211> 18  
 <212> PRT  
 <213> Homo sapiens

<400> 549  
 Leu Glu Ala Leu Leu Ser Asp Leu Phe Arg Asp Pro Asp His Cys Arg  
 5 10 15  
 Gln Ala

<210> 550  
 <211> 14  
 <212> PRT  
 <213> Homo sapiens

<400> 550  
 Ser Asp His Trp Arg Gly Arg Tyr Gly Arg Arg Pro Phe  
 5 10

<210> 551  
 <211> 11  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Made in a lab

<400> 551  
 Phe Asp Lys Ser Asp Leu Ala Lys Tyr Ser Ala  
 5 10

<210> 552  
 <211> 2577  
 <212> DNA  
 <213> Homo sapiens

<400> 552  
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 tcataccagt ccacggacta ttatgaacca caccacacag gaggaggtag gcactaggca 180  
 agccaaggaa gcttcacctg tacttacagc cacacgccat ggctcatatt acagcctgaa 240  
 ctctgcctcc actcagatca gtgataacat tagaaactca ttggagcacg aaccctgttg 300  
 tgaactgcct atccgaagga tctaggttgt gtgcttcgta tgagaatcta atgccagatg 360  
 atctatcatt gtctcacttt gcccccagat aagaccatct agttgcagaa aaataagctc 420  
 agagcttcca ctgattctac attatggata tgtgccgccc aagcaagcac aaagccctac 480  
 ttttacacat gcctagtgat gcttcattga caaggcttgg ctctgttgag tccaactaac 540  
 ctacctgaga ttctgagatt tctcttcaat ggcttctgtg gagctagagt ttgaaaatat 600  
 cttaaaatct tgagctagag atggaagtag cttggacgat tttcattatc atgtaaatcg 660  
 ggtcactcaa ggggccaacc acagctggga gccactgctc aggggaaggt tcatatggga 720  
 ctttctactg cccaagggtt tatacaggat ataaagggtc ctcacagtat agatctggta 780  
 gcaaagaaga agaaacaaac actgatctct ttctgccacc cctctgacct tttggaactc 840  
 ctctgacctt ttagaacaag cctaccta atctgctaga gaaaagacca acaacggcct 900  
 caaaggatct cttaccatga aggtctcagc taattcttgg ctaagatgtg gggtccacat 960

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taggtttctga atatggggggg aagggtcaat ttgtctcatt tgtgtgtgga taaagtcagg 1020
atgcccagg ggcagagcag ggggctgctg ctttggaac aatggctgag catataacca 1080
taggtatggg aacaaaaaac atcaaaagtca ctgtatcaat tgccatgaag actcgaggga 1140
cctgaatcta ccgattcatc ttaaggcagc aggaccagtt tgagtggcaa caatgcagca 1200
gcagaatcaa tggaaacaac agaattgattg caatgtcctt ttttttctcc tccttctgac 1260
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aaagtcctga gataaagaat cctgcaccca ctggtacttc taacttgtct tgttttttgt 1560
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ccacctacgg cttgtcttca ttaaaggaaa agtgtatcca cttaaaaaaa aaaaaaa 2577

```

&lt;210&gt; 553

&lt;211&gt; 58

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 553

```

Ser Ile Cys Asn Met Thr Cys Ala Ser Val Phe Phe Cys Asp Gln Lys
                    5                      10                      15
Phe Leu Thr Phe Ser Phe Leu Ser Met Val Glu Pro Pro Arg Ala Gly
                    20                      25                      30
Val Leu Asn Ser Gln Ala Thr Asp Ser Tyr Gln Ser Thr Asp Tyr Tyr
                    35                      40                      45
Glu Pro His His Thr Gly Gly Gly Glu His
                    50                      55

```

&lt;210&gt; 554

&lt;211&gt; 59

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 554

```

Leu Gln Lys Asn Lys Leu Arg Ala Ser Thr Asp Ser Thr Leu Trp Ile
                    5                      10                      15
Cys Ala Ala Glu Ala Ser Thr Lys Pro Tyr Phe Tyr Thr Cys Leu Val
                    20                      25                      30
Met Leu His Gly Gln Gly Leu Ala Leu Leu Ser Pro Thr Asn Leu Pro
                    35                      40                      45
Glu Ile Leu Arg Phe Leu Phe Asn Gly Phe Leu
                    50                      55

```

197

<210> 555  
 <211> 71  
 <212> PRT  
 <213> Homo sapiens

<400> 555  
 Leu Gly Arg Phe Ser Leu Ser Cys Lys Ser Gly His Ser Arg Gly Gln  
                   5                  10                  15  
 Pro Gln Leu Gly Ala Thr Ala Gln Gly Lys Val His Met Gly Leu Ser  
                   20                  25                  30  
 Thr Ala Gln Gly Ser Ile Gln Asp Ile Lys Val Pro His Ser Ile Asp  
                   35                  40                  45  
 Leu Val Ala Lys Lys Lys Lys Gln Thr Leu Ile Ser Phe Cys His Pro  
                   50                  55                  60  
 Ser Asp Pro Leu Glu Leu Leu  
                   65                  70

<210> 556  
 <211> 81  
 <212> PRT  
 <213> Homo sapiens

<400> 556  
 Asn His Pro Glu Gln Gly Ser Ser Thr Pro Arg Pro Gln Thr His Thr  
                   5                  10                  15  
 Ser Pro Arg Thr Ile Met Asn His Thr Thr Gln Glu Glu Val Ser Thr  
                   20                  25                  30  
 Arg Gln Ala Lys Glu Ala Ser Pro Val Leu Thr Ala Thr Arg His Gly  
                   35                  40                  45  
 Ser Tyr Tyr Ser Leu Asn Ser Ala Ser Thr Gln Ile Ser Asp Asn Ile  
                   50                  55                  60  
 Arg Asn Ser Leu Glu His Glu Pro Cys Cys Glu Leu Pro Ile Arg Arg  
                   65                  70                  75                  80  
 Ile

<210> 557  
 <211> 54  
 <212> PRT  
 <213> Homo sapiens

<400> 557  
 Ser Leu Ser Ala Thr Pro Leu Thr Leu Trp Asn Ser Ser Asp Pro Leu  
                   5                  10                  15  
 Glu Gln Ala Tyr Leu Ile Ser Ala Arg Glu Lys Thr Asn Asn Gly Leu  
                   20                  25                  30  
 Lys Gly Ser Leu Thr Met Lys Val Ser Ala Asn Ser Trp Leu Arg Cys  
                   35                  40                  45  
 Gly Phe His Ile Arg Phe  
                   50

<210> 558  
 <211> 77  
 <212> PRT  
 <213> Homo sapiens

&lt;220&gt;

&lt;221&gt; VARIANT

&lt;222&gt; (1)...(77)

&lt;223&gt; Xaa = Any amino acid

&lt;400&gt; 558

```

Asn Asp Arg Asp Arg Asn Ser Asn Lys Val Ile Xaa Lys Ala Asn Leu
              5              10              15
Ile Tyr Phe Thr Asn Leu Thr Ser Cys Leu Ser Val Gln Asn Gln Thr
              20              25              30
Phe Thr Cys Thr Lys Arg His Lys His Leu Gln Cys Ser Ser Val His
              35              40              45
Leu Cys Lys Ile Pro Pro Arg Leu Lys Gly Arg Asp Lys Lys Lys Lys
              50              55              60
Pro Ser Tyr Leu Ser Gly Val Leu His Ser Arg Ser Tyr
              65              70              75

```

&lt;210&gt; 559

&lt;211&gt; 50

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 559

```

Thr Leu Pro Pro Leu Arg Ser Val Ile Thr Leu Glu Thr His Trp Ser
              5              10              15
Thr Asn Pro Val Val Asn Cys Leu Ser Glu Gly Ser Arg Leu Cys Ala
              20              25              30
Ser Tyr Glu Asn Leu Met Pro Asp Asp Leu Ser Leu Ser His Phe Ala
              35              40              45
Pro Arg
              50

```

&lt;210&gt; 560

&lt;211&gt; 56

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 560

```

Ile Gly Ser Leu Lys Gly Pro Thr Thr Ala Gly Ser His Cys Ser Gly
              5              10              15
Glu Gly Ser Tyr Gly Thr Phe Tyr Cys Pro Arg Phe Tyr Thr Gly Tyr
              20              25              30
Lys Gly Ala Ser Gln Tyr Arg Ser Gly Ser Lys Glu Glu Glu Thr Asn
              35              40              45
Thr Asp Leu Phe Leu Pro Pro Leu
              50              55

```

&lt;210&gt; 561

&lt;211&gt; 57

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; VARIANT

199

&lt;222&gt; (1)...(57)

&lt;223&gt; Xaa = Any amino acid

&lt;400&gt; 561

```

Val Leu His Leu Asp Gln Met Asn Asn Val Gly Ile Xaa Met Asp Lys
                    5              10              15
Gly Leu Lys Ser Pro Glu Ile Lys Asn Pro Ala Pro Thr Gly Thr Ser
                20              25              30
Asn Leu Ser Cys Phe Leu Ser Xaa Phe Trp Leu Met Gln Gly Thr Asn
                35              40              45
Ser Leu Pro Arg Glu Asn Tyr Leu Asn
                50              55

```

&lt;210&gt; 562

&lt;211&gt; 59

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; VARIANT

&lt;222&gt; (1)...(59)

&lt;223&gt; Xaa = Any amino acid

&lt;400&gt; 562

```

Asp Leu Tyr Pro Xaa Arg Ser Gln His Cys Ser Phe Asp Pro Ser Val
                    5              10              15
Ala Pro Met His Gly Ile Lys Asn Ser Ile Thr Ser Leu Ile Phe Leu
                20              25              30
Ile Ser Tyr Leu Xaa Leu Glu Met Ser Ser Leu Ser Glu Ser Leu Val
                35              40              45
Leu Ser Ser Gly Asp Tyr Val Leu Asp Thr Pro
                50              55

```

&lt;210&gt; 563

&lt;211&gt; 79

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 563

```

Cys Phe Leu Phe Pro Tyr Leu Trp Leu Tyr Ala Gln Pro Leu Phe Pro
                    5              10              15
Lys Gln Gln Pro Pro Ala Leu Ala Pro Gly His Pro Asp Phe Ile His
                20              25              30
Thr Gln Asn Glu Gln Ile Asp Pro Ser Pro His Ile Gln Asn Leu Met
                35              40              45
Trp Asn Pro His Leu Ser Gln Glu Leu Ala Glu Thr Phe Met Val Arg
                50              55              60
Asp Pro Leu Arg Pro Leu Leu Val Phe Ser Leu Ala Asp Ile Arg
                65              70              75

```

&lt;210&gt; 564

&lt;211&gt; 64

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 564



200

```

Ala Cys Ser Lys Gly Ser Glu Glu Phe Gln Arg Val Arg Gly Val Ala
      5      10      15
Glu Arg Asp Gln Cys Leu Phe Leu Leu Leu Cys Tyr Gln Ile Tyr Thr
      20      25      30
Val Arg His Leu Tyr Ile Leu Tyr Arg Thr Leu Gly Ser Arg Lys Ser
      35      40      45
His Met Asn Leu Pro Leu Ser Ser Gly Ser Gln Leu Trp Leu Ala Pro
      50      55      60

```

<210> 565  
 <211> 57  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> VARIANT  
 <222> (1)...(57)  
 <223> Xaa = Any amino acid

```

<400> 565
Leu Tyr Tyr Cys Ser Tyr Leu Cys His Phe Arg Thr Ala Leu Ile Leu
      5      10      15
Ala Val Cys Cys Gly Ser Ala Ser Ile Val Ser Leu Leu Glu Gln
      20      25      30
Asn Ile Asp Val Ser Ser Gln Asp Leu Ser Gly Gln Thr Ala Arg Glu
      35      40      45
Tyr Ala Val Ser Ser Xaa His Asn Val
      50      55

```

<210> 566  
 <211> 55  
 <212> PRT  
 <213> Homo sapiens

```

<400> 566
Ile Leu Leu Glu Phe Phe Arg Asn Gln Arg Gly Ser Leu Asn Pro Arg
      5      10      15
Lys Thr Val Pro Phe Ile Lys Ser Glu Gly Gly Glu Lys Lys Gly His
      20      25      30
Cys Asn His Ser Val Val Ser Ile Asp Ser Ala Ala Ala Leu Leu Pro
      35      40      45
Leu Lys Leu Val Leu Leu Pro
      50      55

```

<210> 567  
 <211> 51  
 <212> PRT  
 <213> Homo sapiens

```

<400> 567
Tyr Ser Asp Phe Asp Val Phe Cys Ser His Thr Tyr Gly Tyr Met Leu
      5      10      15
Ser His Cys Ser Gln Ser Ser Ser Pro Leu Leu Trp Pro Leu Gly Ile
      20      25      30
Leu Thr Leu Ser Thr His Lys Met Ser Lys Leu Thr Leu Pro Pro Ile

```

201

35 40 45  
 Phe Arg Thr  
 50  
 <210> 568  
 <211> 75  
 <212> PRT  
 <213> Homo sapiens  
 <400> 568  
 Lys Val Gly Glu Tyr Ile Leu Gln Ser Leu Leu Arg Ile Arg Lys Ile  
 5 10 15  
 Tyr Val Ala Phe Asn Ser Val Pro Ser Thr Cys Leu Leu Ala Ser Leu  
 20 25 30  
 Thr Glu Thr Pro Val Thr Thr Ile Leu Thr Ile Ile Ile Asn Leu Thr  
 35 40 45  
 Cys Phe Gln His Ala Glu Ser Ser Tyr Leu Phe Tyr Pro Leu Ala Asp  
 50 55 60  
 Phe Leu Leu Gln His Ile Ser Leu Gly Lys Leu  
 65 70 75

<210> 569  
 <211> 4809  
 <212> DNA  
 <213> Homo sapiens

<400> 569  
 gcatccagag tgggtggactg gttacaggct atgaacotac actgatgcgg caccaccacc 60  
 cagagtccac rgggttatgtt gggtcacatt tactcttgct gtggtatggg ctatagggtt 120  
 ggacagatgt ccgataatcc tttttacatt ttggcatcct tgggtagctc gtctttagg 180  
 aatggacttg cttcaaagtg gaggcaggca gatccttcag acgggtatat ggagccctgt 240  
 tttcagttgc ttttctaatt ctctcttatt gtttacctca aaatcttctt gaggtctcgc 300  
 ttctttttaa aatccttgct tactttgcag catcactctg acactcccat tgattcctca 360  
 gcacctactg actacacggg taggagtgcagg agggtagaat tcatgtttta ttcattcttg 420  
 ggtctgtagc acccagcaaa gtgctcagta aatgcgcagt aattgatttg acctctgaac 480  
 aaatacacac tgtactaaga atctacacac cgaaagacaa aaacaagaca aatttgagtg 540  
 ctacaggtgt cacgcttggt atcacacatg tgcctgtgta ttctcttagg tgggtaccag 600  
 gagctctgac actgcattgc cactagtgcagg ggggttcgctc caccacccca gctgggtagc 660  
 cgctgctctc acataagggg tccaattaaa attgccagga ataaattccc ccggactttg 720  
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aaaaaaaaa 4809

```

&lt;210&gt; 570

&lt;211&gt; 951

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 570

203

```

aaaattgaat attgagatac cattctttag tgttaccttt tttaccacaca tgtgtttctg 60
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```

&lt;210&gt; 571

&lt;211&gt; 819

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 571

```

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aaataaacia acaaacacaa aaaacagaga gattttgct 819

```

&lt;210&gt; 572

&lt;211&gt; 203

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 572

```

tatagaatac tcaagctatg catcaagctt ggtaccgagc tcggatccac tatttacggc 60
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attgtgttgg gcccaacaca atggagccac cacatccagc ctgccacata cttttaaact 180
atcaggctc atgagaactc atg 203

```

&lt;210&gt; 573

&lt;211&gt; 132

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 573

```

Met Val Glu Gly Glu Gly Glu Ala Arg His Val Leu His Gly Gly Arg
          5              10              15
Arg Glu Arg Val Arg Gly Glu Thr Ala Thr Asn Phe Phe Phe Leu Arg

```

204

```

      20      25      30
Gln Glu Ser Gly Pro Val Ala Gln Ala Gly Val Gln Trp His Asp Leu
      35      40      45
Ser Ser Leu Gln Pro Leu Pro His Arg Phe Lys Gln Phe Ser Cys Leu
      50      55      60
Ser Leu Pro His Ser Trp Asp His Arg Tyr Ala Pro Pro His Leu Ala
      65      70      75      80
Asn Phe Cys Ser Phe Ser Arg Asp Gly Val Ser Leu Cys Cys Ser Gly
      85      90      95
Trp Ser Lys Thr Pro Gly Leu Gln Gln Ser Ala Cys Leu Gly Leu Pro
      100      105      110
Lys Cys Trp Gly Tyr Arg His Lys Pro Pro His Pro Ala Cys His Ile
      115      120      125
Leu Leu Asn Tyr
      130

```

<210> 574  
 <211> 62  
 <212> PRT  
 <213> Homo sapiens

```

<400> 574
Met Thr His Ser Ser Ala Trp Leu Glu Arg Pro Gln Glu Thr Tyr Asn
      5      10      15
His Gly Gly Arg Arg Arg Gly Ser Lys Ala Arg Leu Thr Trp Trp Gln
      20      25      30
Glu Arg Thr Ser Glu Gly Gly Asp Cys His Lys Leu Phe Phe Glu
      35      40      45
Thr Arg Val Trp Pro Cys Cys Pro Gly Trp Ser Ala Val Ala
      50      55      60

```

<210> 575  
 <211> 76  
 <212> PRT  
 <213> Homo sapiens

```

<400> 575
Met Val Lys Ser Arg Phe Thr Lys Asn Thr Lys Ile Thr Gln Ala Trp
      5      10      15
Trp Arg Ala Pro Val Ile Pro Gly Thr Arg Glu Ala Glu Gly Glu
      20      25      30
Ser Leu Glu Pro Gly Arg Leu Arg Glu Glu Asn Arg Leu Asn Pro Gly
      35      40      45
Gly Arg Gly Cys Ser Glu Pro Arg Ser Cys Cys Cys Thr Pro Ala Trp
      50      55      60
Ser Thr Glu Gln Asp Ser Ala Ser Lys Thr Asn Lys
      65      70      75

```

<210> 576  
 <211> 68  
 <212> PRT  
 <213> Homo sapiens

<220>  
 <221> VARIANT

205

&lt;222&gt; (1)...(68)

&lt;223&gt; Xaa = Any Amino Acid

&lt;400&gt; 576

```

Met Leu Gly Lys Ser Arg Ala Val Cys Leu Pro Ser Thr Thr Val Thr
      5              10              15
Thr Val Cys Tyr Leu Ala Ser Ser Ser Ala Ser Arg Glu Thr Ala Thr
      20              25              30
Arg Gln Ala Pro Gly Asn Trp Lys Met Xaa Ser Lys Cys His Ala Gln
      35              40              45
Leu Leu Phe Thr Phe Tyr Leu Asn His Phe Tyr Gln Ile Arg Leu Asn
      50              55              60
Pro Gly Tyr Ser
65

```

&lt;210&gt; 577

&lt;211&gt; 57

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 577

```

Met Tyr Leu Glu Asn Ser Phe Tyr Cys Gln Met Ile Leu Leu Lys Arg
      5              10              15
Cys Arg Leu Ser Lys Ile Ser Thr Gln Arg Val Val Pro Asp Gly Pro
      20              25              30
Pro Ala Pro Val Pro Gly Ser Phe Pro Met Phe Pro Arg Phe Gly Phe
      35              40              45
Arg Leu Ala Pro Pro Ala Asp Thr Pro
      50              55

```

&lt;210&gt; 578

&lt;211&gt; 51

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 578

```

Met Gln Leu Ile Tyr Leu Cys Phe Leu Gly Leu Leu Tyr Ile Arg His
      5              10              15
His Asp Ser Gln Ser Phe Val Ile Leu Tyr Tyr Lys Lys Leu Asn Tyr
      20              25              30
Tyr Phe Lys Tyr Gly Gln Ile Arg Ala Phe His Ile Ala Lys Val Tyr
      35              40              45
Gln Pro His
50

```

&lt;210&gt; 579

&lt;211&gt; 56

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 579

```

Met His Phe Thr Phe Met Gln Leu Ile Tyr Leu Cys Phe Leu Gly Leu
      5              10              15
Leu Tyr Ile Arg His His Asp Ser Gln Ser Phe Val Ile Leu Tyr Tyr
      20              25              30
Lys Lys Leu Asn Tyr Tyr Phe Lys Tyr Gly Gln Ile Arg Ala Phe His
      35              40              45
Ile Ala Lys Val Tyr Gln Pro His

```

206

50

55

&lt;210&gt; 580

&lt;211&gt; 67

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 580

```

Met Glu Leu Arg Thr Lys Ala Leu Arg Thr Ala Gln Gln Leu Thr Ser
      5              10              15
Cys Val Thr Ala Leu Lys Ala Ala Gly Pro Pro Leu Thr Phe Trp Lys
      20              25              30
Gly Lys Trp Val Gln Cys Cys Leu Pro Leu Trp Gly Leu Leu Gly Ser
      35              40              45
His Ala Phe Tyr Ile Tyr Ala Val Asp Ile Phe Met Phe Pro Gly Ser
      50              55              60
Phe Ile His
      65

```

&lt;210&gt; 581

&lt;211&gt; 77

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 581

```

Met Leu Glu Val Lys Phe Glu Val Ser Leu Arg Pro Thr Gly Asn Glu
      5              10              15
Thr Ala Gly Gln Thr His Gly Thr Gln Asp Lys Gly Ser Lys Asp Ser
      20              25              30
Thr Ala Ala Asp Ile Leu Cys Asp Ser Leu Glu Ser Ser Arg Pro Ala
      35              40              45
Ala His Ile Leu Glu Gly Lys Met Gly Thr Met Leu Ser Ala Thr Leu
      50              55              60
Gly Pro Ser Trp Val Thr Cys Ile Leu His Leu Cys Ser
      65              70              75

```

&lt;210&gt; 582

&lt;211&gt; 51

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 582

```

Met Leu Phe Leu Gln Thr Ile Asp Thr Lys Cys Thr Gly Ile Glu Ile
      5              10              15
Asn Arg Asn Trp Ser Lys Val Trp His Thr His Ser His Val Asp Val
      20              25              30
Lys Leu Cys Leu Glu Phe Leu Cys Gly Val Trp Phe Gly Leu Gly Phe
      35              40              45
Leu Gly Val
      50

```

&lt;210&gt; 583

&lt;211&gt; 60

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 583

```

Met Ser Thr Ser Asp Gly Phe Ala Pro Pro Pro Gln Leu Gly Ser Arg

```

207

```

      5          10          15
Cys Ser His Ile Arg Gly Pro Ile Lys Ile Ala Arg Asn Lys Phe Pro
      20          25          30
Arg Thr Leu Thr Ser Gln Glu Leu Arg Arg Phe Ala Glu Tyr Ser Gly
      35          40          45
Met Met Phe Gly Asp Gln Thr Thr Ala Gly Gln Lys
      50          55          60

```

<210> 584  
 <211> 76  
 <212> PRT  
 <213> Homo sapiens

```

<400> 584
Met Cys Leu Cys Ile Pro Leu Gly Gly Tyr Gln Glu Leu Cys His Cys
      5          10          15
Met Ser Thr Ser Asp Gly Phe Ala Pro Pro Pro Gln Leu Gly Ser Arg
      20          25          30
Cys Ser His Ile Arg Gly Pro Ile Lys Ile Ala Arg Asn Lys Phe Pro
      35          40          45
Arg Thr Leu Thr Ser Gln Glu Leu Arg Arg Phe Ala Glu Tyr Ser Gly
      50          55          60
Met Met Phe Gly Asp Gln Thr Thr Ala Gly Gln Lys
      65          70          75

```

<210> 585  
 <211> 50  
 <212> PRT  
 <213> Homo sapiens

```

<400> 585
Met Val Tyr Arg Phe Gly Gln Met Ser Asp Asn Pro Phe Tyr Ile Leu
      5          10          15
Ala Ser Leu Gly Ser Ser Ser Cys Arg Asn Gly Leu Ala Ser Lys Trp
      20          25          30
Arg Gln Ala Asp Pro Ser Asp Gly Tyr Met Glu Pro Cys Phe Gln Leu
      35          40          45
Leu Phe
      50

```

<210> 586  
 <211> 60  
 <212> PRT  
 <213> Homo sapiens

```

<400> 586
Met Leu Val His Ile Tyr Ser Cys Cys Gly Met Val Tyr Arg Phe Gly
      5          10          15
Gln Met Ser Asp Asn Pro Phe Tyr Ile Leu Ala Ser Leu Gly Ser Ser
      20          25          30
Ser Cys Arg Asn Gly Leu Ala Ser Lys Trp Arg Gln Ala Asp Pro Ser
      35          40          45
Asp Gly Tyr Met Glu Pro Cys Phe Gln Leu Leu Phe
      50          55          60

```

<210> 587  
 <211> 1408  
 <212> DNA



&lt;213&gt; Homo sapiens

&lt;400&gt; 587

```

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```

&lt;210&gt; 588

&lt;211&gt; 81

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 588

```

Met Pro Gln Lys Gln Gln Asn Ser Gln Thr Glu Ala Lys Tyr Arg Ala
                    5                      10                      15
Leu Gln Phe Arg Gln Tyr Asn Lys Ser Val His Glu Val Asn Leu Lys
                    20                      25                      30
Gly Ala Cys Phe Thr Val Ala Gly Leu Pro Arg Ala Trp Thr Thr Gln
                    35                      40                      45
Tyr Ser Ile Ile Asp Lys Arg Ile Arg Gln Glu Ile Tyr Thr Cys Cys
                    50                      55                      60
Leu Ala Phe Val Val Ile Tyr Thr Asn Glu Asn Met Tyr Tyr Ser Tyr
                    65                      70                      75                      80
Ile

```

&lt;210&gt; 589

&lt;211&gt; 157

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 589

```

Met Thr Met Cys Leu Cys Val Ala Pro Met Gly Arg Ala Thr Arg Met
                    5                      10                      15
Ser Val Thr Cys Asp Arg Leu His Ala Asn Ser Arg Val Arg Tyr Leu
                    20                      25                      30
Trp Cys Gln Lys Asp His Val Pro Gln Met Gln Asp Gln Asp Leu Glu

```

209

```

      35          40          45
Met Glu Ser Met Lys Ala Leu Glu Lys Leu Val Lys Arg Arg His Pro
   50          55          60
Pro Val Ile Phe Ala Ser Leu Val Gln Asn Val Thr Lys Met Pro Arg
   65          70          75          80
Met Ser Gly Val Cys Val Ile Leu Thr Val Leu Lys Pro Thr Ser Ile
      85          90          95
Pro Ser Ala Leu Leu Met Gly Asn Leu Met Ile Met His Ala Lys Ser
      100          105          110
Lys Lys His Arg Val Arg Asn Arg Arg Lys Leu Lys Ser Cys Leu Trp
      115          120          125
Val Asp Val Lys Ile Thr Gln Leu Gln Leu Leu Ser Leu Lys Met Gly
      130          135          140
Ile Met Gln Glu Gln Ile Met Gln Arg Met Leu Thr Asn
145          150          155

```

&lt;210&gt; 590

&lt;211&gt; 347

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 590

```

Met Leu Leu Ile Val Ala Arg Pro Val Lys Leu Ala Ala Phe Pro Thr
      5          10          15
Ser Leu Ser Asp Cys Gln Thr Pro Thr Gly Trp Asn Cys Ser Gly Tyr
      20          25          30
Asp Asp Arg Glu Asn Asp Leu Phe Leu Cys Asp Thr Asn Thr Cys Lys
      35          40          45
Phe Asp Gly Glu Cys Leu Arg Ile Gly Asp Thr Val Thr Cys Val Cys
      50          55          60
Gln Phe Lys Cys Asn Asn Asp Tyr Val Pro Val Cys Gly Ser Asn Gly
      65          70          75          80
Glu Ser Tyr Gln Asn Glu Cys Tyr Leu Arg Gln Ala Ala Cys Lys Gln
      85          90          95
Gln Ser Glu Ile Leu Val Val Ser Glu Gly Ser Cys Ala Thr Asp Ala
      100          105          110
Gly Ser Gly Ser Gly Asp Gly Val His Glu Gly Ser Gly Glu Thr Ser
      115          120          125
Gln Lys Glu Thr Ser Thr Cys Asp Ile Cys Gln Phe Gly Ala Glu Cys
      130          135          140
Asp Glu Asp Ala Glu Asp Val Trp Cys Val Cys Asn Ile Asp Cys Ser
145          150          155          160
Gln Thr Asn Phe Asn Pro Leu Cys Ala Ser Asp Gly Lys Ser Tyr Asp
      165          170          175
Asn Ala Cys Gln Ile Lys Glu Ala Ser Cys Gln Lys Gln Glu Lys Ile
      180          185          190
Glu Val Met Ser Leu Gly Arg Cys Gln Asp Asn Thr Thr Thr Thr
      195          200          205
Lys Ser Glu Asp Gly His Tyr Ala Arg Thr Asp Tyr Ala Glu Asn Ala
      210          215          220
Asn Lys Leu Glu Glu Ser Ala Arg Glu His His Ile Pro Cys Pro Glu
225          230          235          240
His Tyr Asn Gly Phe Cys Met His Gly Lys Cys Glu His Ser Ile Asn
      245          250          255
Met Gln Glu Pro Ser Cys Arg Cys Asp Ala Gly Tyr Thr Gly Gln His
      260          265          270
Cys Glu Lys Lys Asp Tyr Ser Val Leu Tyr Val Val Pro Gly Pro Val

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210

```

      275      280      285
Arg Phe Gln Tyr Val Leu Ile Ala Val Ile Gly Thr Ile Gln Ile
      290      295      300
Ala Val Ile Cys Val Val Val Leu Cys Ile Thr Arg Lys Cys Pro Arg
      305      310      315      320
Ser Asn Arg Ile His Arg Gln Lys Gln Asn Thr Gly His Tyr Ser Ser
      325      330      335
Asp Asn Thr Thr Arg Ala Ser Thr Arg Leu Ile
      340      345

```

<210> 591  
 <211> 565  
 <212> DNA  
 <213> Homo sapien

```

<400> 591
actaaagcaa atgaacaagc tgacttgcta gtatcatctg cattcattga agcacaagaa      60
cttcatgcct tgactcatgt aaatgcaata ggattaaaaa ataaatttga tatcacatgg      120
aaacagacaa aaaatattgt acaacattgc acccagtgtc agattctaca cctggccact      180
caggaagcaa gagttaatcc cagaggtcta tgtcctaatt tggtatggca aatggatgtc      240
atgcacgtac cttcatttgg aaaattgtca tttgtccatg tgacagttag tacttattca      300
catttcatat gggcaacctg ccagacagga gaaagtactt cccatgttaa aagacattta      360
ttatcttgtt ttcctgtcat gggagttcca gaaaaagtta aaacagacaa tgggccaggt      420
tactgtagta aagcatttca aaaattctta aatcagtggg aaattacaca tacaatagga      480
attctctata attccaagg acaggccata attgaaggaa ctaatagaac actcaaagct      540
caattgttta aacaaaaaaaa aaaaaa      565

```

<210> 592  
 <211> 188  
 <212> PRT  
 <213> Homo sapien

```

<400> 592
Thr Lys Ala Asn Glu Gln Ala Asp Leu Leu Val Ser Ser Ala Phe Ile
  1      5      10      15
Glu Ala Gln Glu Leu His Ala Leu Thr His Val Asn Ala Ile Gly Leu
      20      25      30
Lys Asn Lys Phe Asp Ile Thr Trp Lys Gln Thr Lys Asn Ile Val Gln
      35      40      45
His Cys Thr Gln Cys Gln Ile Leu His Leu Ala Thr Gln Glu Ala Arg
      50      55      60
Val Asn Pro Arg Gly Leu Cys Pro Asn Val Leu Trp Gln Met Asp Val
      65      70      75      80
Met His Val Pro Ser Phe Gly Lys Leu Ser Phe Val His Val Thr Val
      85      90      95
Asp Thr Tyr Ser His Phe Ile Trp Ala Thr Cys Gln Thr Gly Glu Ser
      100      105      110
Thr Ser His Val Lys Arg His Leu Leu Ser Cys Phe Pro Val Met Gly
      115      120      125
Val Pro Glu Lys Val Lys Thr Asp Asn Gly Pro Gly Tyr Cys Ser Lys
      130      135      140
Ala Phe Gln Lys Phe Leu Asn Gln Trp Lys Ile Thr His Thr Ile Gly
      145      150      155      160
Ile Leu Tyr Asn Ser Gln Gly Gln Ala Ile Ile Glu Gly Thr Asn Arg
      165      170      175
Thr Leu Lys Ala Gln Leu Val Lys Gln Lys Lys Lys
      180      185

```

<210> 593  
 <211> 271  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(271)  
 <223> n = A,T,C or G

<400> 593  
 actttatgtt cnagtgcana aanccnctg gattgccacc ntactctcag ggctgtgant 60  
 tgtgcnccca nagcaacctg ggcacgcggg gacagggggg ccnacaattg agggagcggt 120  
 gtccctagct ggggtctata catgncnggg naagggcngc tgagtnccat nagcaaagga 180  
 nctagnatnt gcgggggtgc ggcctgggcc taccctttna agcatcentn gatccactcc 240  
 angaancng gggtagncag gtttnccaac a 271

<210> 594  
 <211> 376  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(376)  
 <223> n = A,T,C or G

<400> 594  
 cctttggggg nggggggaac ctttaccatt gtnccctttt atttcatttg gttngggttc 60  
 gcgccctcnn gggccaacaa agttatcgtn ntgaagaga anattttttt ggnttngncc 120  
 cgattaagcg ncaaatgtgt agcaaaangc cgtgccactt gtggcgtagc tncgtcgggt 180  
 cgattcgacg acaaggcgtn gcgcgntanc gttagtctcn aatngaccen gtggcatgag 240  
 cccacgangg nttcgtgtcg tcacatggnc tctagacata acgcnncn ttttttnacg 300  
 agggggntgc cgcccttagg gaggnagggg tggggacact agccaancca nantctnacc 360  
 ccattgaaga aaaggn 376

<210> 595  
 <211> 242  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(242)  
 <223> n = A,T,C or G

<400> 595  
 agnctgctgn tcgtncctn tatgtggctt catnntgagg acaanagtng cactgaggct 60  
 tgngnatgcc aggcaaggnc aagctggctc aaaaagcatc caccacctc tgnaanggg 120  
 atgccangag cangtgcacc agtcccaact angagnccn ggcatgntac atcttcttcc 180  
 acccctnaaa ntttngcta caangnccat ttttctttt ctcttaaggg ncnctggct 240  
 tc 242

<210> 596  
 <211> 535  
 <212> DNA  
 <213> Homo sapien

212

```

<220>
<221> misc_feature
<222> (1)...(535)
<223> n = A,T,C or G

<400> 596
accagttgga tactgctaaa nagatattha tgcagcctca tatgttaagt cgtatatattt    60
gaaagctttt taaatttttt ctttaagaag attttagatg cttatcactg agtaccagag    120
ggatgtaggc tgatgccctt atcaacaaag tcagggactg tggcacacaa ggattgacta    180
ctgcagacac ggccacaatg ctacctctag agggcctgaa tcccctgcc ctctctgggtg    240
gggagaaggg ctggcagagc cattagcatg ggctccggcc aatcctggcc actttgacac    300
tcctggtgct gacccagggt cctggaggaa gggatgaggt gggcagtaga gatgctcagg    360
gcagtggccc ctttccatcc aacttggaac tatttcagta ttttaccacc aattcagcca    420
ttcccttgct cgctggctga acatcagccc tgctccaggt ctcagtttcc cctttgtaaa    480
gggaaagctc tggattcagg gagtgatgaa gaggtcatca tggctcttgag aattc      535

<210> 597
<211> 257
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(257)
<223> n = A,T,C or G

<400> 597
tttcnatacc caaaantacc ccatattang accanacatt tgcctnngaa aaattaccat    60
tntntaacnt ttgggccacc tgagannaaa tgggtgtaat ncatgataag atggancagn    120
attnctctta agatnngatn agaccccggt ttacacggaa catatccaag nacccaatag    180
gnaacaagcc acgggnggag tcacaaacat atattcttta ctctcataat ccgtnnacac    240
naactnttgn acttgac      257

<210> 598
<211> 222
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(222)
<223> n = A,T,C or G

<400> 598
nntggntacc gtcnaaactt nncttggtac ccgagctcgg atccactagt ccagtgtggt    60
ggaattccat tgtgttgggc tataagctgt aatagtggag ncgtgctngg ttcattgcan    120
nagnccctcc gcanncacnc ttgnnacaac ctgtgagnag gcnataaatt attcacataa    180
tcatactgc atgaanctga ctcaaacgca tccacntaca cc      222

<210> 599
<211> 238
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(238)

```

213

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 599

gcatgacatc	ancgatgtnt	ttggnnacct	ganattngct	aaaactngng	natgccgggn	60
atgnagggtt	ggtantgatc	tatgcactca	catctcatgg	ggacgtttca	tgtggagtgn	120
tcgacaangt	tgctgnannc	gagaagtgat	gatctcagtt	gaaagggcca	tgtgaataca	180
cnttacactt	gaaaaagaag	cacattggga	atatcacgaa	acgnccacca	acatcctg	238

&lt;210&gt; 600

&lt;211&gt; 232

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(232)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 600

cgaactattt	agactaccta	ggaaaattat	tttagtatca	gaagaatata	aggggtgtag	60
tactcatcag	agctaaatga	gagcgcttta	aaaatgttag	tttgtcttcc	gccatttcta	120
cagaaagctg	caatttcagg	ttttcaacct	aataggtgat	atttaaaaaa	aaaaaaaagc	180
aatcgcaaat	agccccactg	cttttacaac	tcattttttc	cccaacacaa	tg	232

&lt;210&gt; 601

&lt;211&gt; 547

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(547)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 601

cattgtgttg	gggaaaaaat	gatttgtata	agcagtgggg	ctatttgcca	ttgctttttt	60
tttttcttaa	atatcaccta	ttaggttgaa	aacctgaaat	tgcagctttc	tgtagaaatg	120
gcggaagaca	aactaacatt	tttaaagcgc	tctcatctag	ctctgatgag	tactacaccc	180
ctnatattct	tctgatacta	aaataatttt	cctagtgtag	tctaaacttt	tttaaaaaga	240
catgtaatcc	gcggagttag	taactcaaaa	cgagtgcata	tnggaagtat	cgcagccggt	300
nctggatnaa	attcccagct	tgctngcttg	ctnagccggg	gggaggtnaa	aaaaacatct	360
gcagcccnng	ggnaaaaacc	ttcgcatgtt	tcttacgtgt	ttacgttatt	ttatttcctt	420
nnagcaaggc	nggganttgg	ggactcgaaa	tggtacagtt	gggctgggga	tcgcccttgt	480
tacataaaaag	ncgtccagaa	gagggacggt	tacaggcnng	ganctccaaa	ggtcagtcct	540
tgccatt						547

&lt;210&gt; 602

&lt;211&gt; 826

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(826)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 602

cggggggnnt	tacgtctctc	tggaagcttt	tattgtacca	gggcgatccc	agcccaactg	60
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214

taccatttcga	gtccctactc	ctgccttgct	ctagggaat	aaaataacgt	aaacacgtaa	120
gaacaatgcg	aaagcgtttt	cttccctagg	ctgcagattg	tcttcttcac	cgccctgct	180
tagctagcta	gctagctggg	aatttaatcc	agaaacggct	tgcgatacct	cctagatgca	240
ctcgttttga	gttacaaact	ccgcggatta	catgtctttt	taaaaaagtt	tagactacac	300
tagggaaaat	tatttttagta	tcagaagaat	atcagggggt	gtagtactca	tcagagctna	360
atgagagcgc	tttaaaaatg	ttagtttgct	ttccgccatt	tctacagaaa	gctgcaattt	420
cagggttttca	ncctaatagg	tgatatntaa	gaaaaaaaaa	acaatcgcan	atagccact	480
gctttttacaa	atcatttttc	tcttctaggt	atagcctgtc	aggtggccta	atgtattttt	540
gacatctcta	ggaattttta	tagaccagaa	atgggtgccca	gagatatgcc	tgactaatac	600
ttaagtgggg	atttatgtat	ttctcaanca	agtgattaaa	gcaaaactag	gcacgaatga	660
aatcaagatc	tttaggccag	aaatcatgaa	nanttttana	attattttan	gaatctgtgg	720
cttctcttct	taaaatngaa	aaaaaaattg	tttaaacccta	naaggtctga	ataccaagc	780
ncctgaacn	anagaacaan	gccggagcac	cccctcccaa	atcccc		826

&lt;210&gt; 603

&lt;211&gt; 817

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(817)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 603

nnangacttt	tgtggtntta	tacaattntt	ttttctatit	ctatgaagag	aaagccacag	60
agtcctaaaa	taattctaaa	actcatcatg	actttcttgc	ctaaaagatc	ttgatttcaa	120
tcgtgcctag	ttttgcttta	atcacttgct	tgagaaatac	ataaatcccc	acttaagatt	180
agtgacaggca	tatctctggc	acccatttct	ggttctatta	aaattcctag	agatgtcaaa	240
aattacatta	ggccacctga	caggctatac	ctagaagaga	aaaaatgatt	tgtaaaagca	300
gtggggctat	ttgcgattgc	tttttttttt	tottaaatat	cacctattag	gttgaaaacc	360
tgaaattgca	gctttctgta	gaaatggcgg	aagacaaact	aacattttta	aagcgctctc	420
atttagctct	gatgagtact	acacccctga	tattctcttg	atactaaaa	aattttccta	480
gtgtagtcta	aactttttta	aaaagacatg	taatccgagg	agtttgtaac	tcaaaacgag	540
tgcatctagg	aggtatcgca	agccgtttct	ggattaaatt	cccagctagc	ttgcttgctt	600
agcagggggc	ggnaaanaag	acatctgcag	cctagggaag	aaaacctttc	gcattgttct	660
tacgtgttta	cgttatttta	tttctctana	caaggcngaa	ttgggactcg	aatggttcag	720
ttgggggtgg	ggatccctcg	gtncataaaa	ngtcanaaag	anggtacagg	cggaaaccca	780
agggctcgcc	tgcatttana	ctcggaattt	tggtgcc			817

&lt;210&gt; 604

&lt;211&gt; 694

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(694)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 604

cttttcaa	at	catttttnt	cttctaggta	tancctgtca	gggtggcctaa	tgtaattttt	60
gacatctcta	ngaattttta	tagaaccaga	aatgggtgcc	agagatatgc	ctgcactaat		120
cttaagtggg	gatttatgta	tttctcaagc	aagtgtatga	agcaaaacta	ggcacgattg		180
aaatcaagat	cttttaggca	anaaagtcat	gatgagtttt	agaattattt	taggactctg		240
tggttttctc	ttcatagaaa	tagaaaaaaa	aattgtataa	aaccacaaaa	ggtcctgaat		300
agccaaagca	acactganca	aaaagaacan	agcaggggaag	caacacacta	cnngaattca		360
aattatacta	ccaggggtgta	gtaacaaaaa	cagcattcta	ttggcataaa	atagacacca		420

215

```

agaccaatgg ancagaataa agaacccccc aaataaatcc atatatntac cgccanctga 480
ttatcaataa cnaacaccaa gaacatatnt taaggacnt nctattcaat aantagtgtc 540
ggnaaaaact gggaaatcca tatgcagaaa naatgaaact agacccttat ccctcaccat 600
acgcaaannt caacttcgga atgggattac aaaacttaag acattccaac ccaagaaact 660
atnaaancta ctattaagaa aacagatcnc nccc 694

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```

<210> 605
<211> 678
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(678)
<223> n = A,T,C or G

```

```

<400> 605
taaaaatcta gactacacta ggaaattatt ttantatcag aagaatatca ggggtgtagt 60
actcatcana gctaaatgag agcgctttaa aaatgttagt ttgtcttccg ccatttctac 120
agaaagctgc aatttcagggt ttccaaccta atagggtgata tttaagaaaa aaaaaagca 180
atcgcaataa gccccactgc ttttacaat catTTTTtct cttctaggta tagcctgtca 240
ggtggcctaa tgtaattttt gacatctcta ggaattttta tagaaccaga aatgggtgcc 300
agagatatgc ctgcactaat cttaagtggg gatTTatgta tttctcaagc aagtgattaa 360
agcaaaacta ggcacgattg aaatcaanat cttttaggca agaaagtcat gatgagtttt 420
anaattattt taggactctg tggctttctc ttcatagaaa tagaaaaaaa aaattgtata 480
aaaaccacaa aaggctcctga atagcccaaa gcaacactga acaaaaangaa caaagcagga 540
agcaacacac taccggaatt caattatact accaagggtg antaaccaaa acagcattct 600
attgggcata aaatagacca aagaccagtg ggaaacagaa taaagaancc caaaataaat 660
cctatattta cngccccc 678

```

```

<210> 606
<211> 263
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(263)
<223> n = A,T,C or G

```

```

<400> 606
gtgggggtcng cancagccaa ctcagcttcc ttctgggctt tgtagcaga cggatcatcc 60
tctagtccac tgtgntcaaa ttccattgtg tgggggccnc tcgcctcggc canagatctg 120
agtgancana cntgtcccca ctgagggtgcc ccacagcngn ttgnttcag cangggctna 180
caactcgacc ggcagcgnan ggctggcaga antgngcgcc tnnctcattc ctacgcngtn 240
ngccgcagga aggangacag gcc 263

```

```

<210> 607
<211> 22
<212> DNA
<213> Artificial Sequence

```

```

<220>
<223> Primer

```

```

<400> 607
ccatgtgggt cccggttggt tt

```

22



216

<210> 608  
<211> 22  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Primer

<400> 608  
gataggggtg ctcaggggtt gg 22

<210> 609  
<211> 40  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Primer

<400> 609  
gctggacagg gggcaaaagc tggggcagtg aaccatgtgc 40

<210> 610  
<211> 27  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Primer

<400> 610  
ccttgtccag atagcccagt agctgac 27

<210> 611  
<211> 46  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Primer

<400> 611  
gatagagaaa accgtccagg ccagtattgt gggaggctgg gagtgc 46

<210> 612  
<211> 40  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Primer

<400> 612  
gcacatggtt cactgccccca gcttttgccc cctgtccagc 40

<210> 613  
<211> 38  
<212> DNA

<213> Artificial Sequence

<220>

<223> Primer

<400> 613

ggcgctcgag ttagaattcg gggttggcca cgatgggtg

38

<210> 614

<211> 53

<212> DNA

<213> Artificial Sequence

<220>

<223> Primer

<400> 614

cggcgggcat atgcatcacc atcaccatca catcataaac ggcgaggact gca

53

<210> 615

<211> 46

<212> DNA

<213> Artificial Sequence

<220>

<223> Primer

<400> 615

gcactcccag cctccacaaa tactggcctg gacggttttc tctatc

46

<210> 616

<211> 1350

<212> DNA

<213> Homo sapien

<400> 616

atgcatcacc atcaccatca catcataaac ggcgaggact gcagcccga ctgcagccc	60
tggcaggcgg cactgggtcat ggaaaacgaa ttgttctgct cgggcgctcct ggtgcatccg	120
cagtgggtgc tgtcagccgc aactgtttc cagaactcct acaccatcgg gctgggctg	180
cacagtcttg aggcgacca agagccaggg agccagatgg tggaggccag cctctccgta	240
cggcaccag agtacaacag acccttgctc gctaacgacc tcatgctcat caagttggac	300
gaatccgtgt ccgagtctga caccatccgg agcatcagca ttgcttcgca gtgccctacc	360
gcggggaact cttgcctcgt ttctggctgg ggtctgctgg cgaacggcag aatgcctacc	420
gtgctgcagt gcgtgaacgt gtccgtgggt tctgaggagg tctgcagtaa gctctatgac	480
ccgctgtacc accccagcat gttctgcgcc ggcggagggc aagaccagaa ggactcctgc	540
aacggtgact ctggggggcc cctgatctgc aacgggtact tgcagggcct tgtgtctttc	600
ggaaaagccc cgtgtggcca agttggcgtg ccagggtgtct acaccaacct ctgcaaattc	660
actgagtgga tagagaaaac cgtccaggcc agtattgtgg gaggtggga gtgcgagaag	720
cattcccaac cctggcagggt gcttgggcc tctcgtggca gggcagctctg cggcgggtgtt	780
ctggtgcacc ccagtggtg cctcacagct gccactgca tcaggaacaa aagcgtgatc	840
ttgctgggtc ggcacagcct gtttcatcct gaagacacag gccagggtatt tcaggtcagc	900
cacagcttcc cacaccgct ctacgatatg agcctcctga agaatcgatt cctcaggcca	960
ggtgatgact ccagccacga cctcatgctg ctccgcctgt cagagcctgc cgagctcacg	1020
gatgctgtga aggtcatgga cctgcccacc caggagccag cactggggac cacctgctac	1080
gcctcaggct gggcagcat tgaaccagag gagttcttga cccaaagaa acttcagtgt	1140
gtggacctcc atgtatttc caatgacgtg tgtgcgcaag ttcaccctca gaaggtgacc	1200
aagttcatgc tgtgtgctgg acgctggaca gggggcaaaa gctggggcag tgaaccatgt	1260
gccctgcccg aaaggccttc cctgtacacc aagtggtgac attaccggaa gtggatcaag	1320

218

gacaccatcg tggccaaccc cgaattctaa

1350

&lt;210&gt; 617

&lt;211&gt; 449

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 617

```

Met His His His His His His Ile Ile Asn Gly Glu Asp Cys Ser Pro
 1          5          10          15
His Ser Gln Pro Trp Gln Ala Ala Leu Val Met Glu Asn Glu Leu Phe
          20          25          30
Cys Ser Gly Val Leu Val His Pro Gln Trp Val Leu Ser Ala Ala His
          35          40          45
Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu Gly Leu His Ser Leu Glu
          50          55          60
Ala Asp Gln Glu Pro Gly Ser Gln Met Val Glu Ala Ser Leu Ser Val
          65          70          75          80
Arg His Pro Glu Tyr Asn Arg Pro Leu Leu Ala Asn Asp Leu Met Leu
          85          90          95
Ile Lys Leu Asp Glu Ser Val Ser Glu Ser Asp Thr Ile Arg Ser Ile
          100          105          110
Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly Asn Ser Cys Leu Val Ser
          115          120          125
Gly Trp Gly Leu Leu Ala Asn Gly Arg Met Pro Thr Val Leu Gln Cys
          130          135          140
Val Asn Val Ser Val Val Ser Glu Glu Val Cys Ser Lys Leu Tyr Asp
          145          150          155          160
Pro Leu Tyr His Pro Ser Met Phe Cys Ala Gly Gly Gln Asp Gln
          165          170          175
Lys Asp Ser Cys Asn Gly Asp Ser Gly Gly Pro Leu Ile Cys Asn Gly
          180          185          190
Tyr Leu Gln Gly Leu Val Ser Phe Gly Lys Ala Pro Cys Gly Gln Val
          195          200          205
Gly Val Pro Gly Val Tyr Thr Asn Leu Cys Lys Phe Thr Glu Trp Ile
          210          215          220
Glu Lys Thr Val Gln Ala Ser Ile Val Gly Gly Trp Glu Cys Glu Lys
          225          230          235          240
His Ser Gln Pro Trp Gln Val Leu Val Ala Ser Arg Gly Arg Ala Val
          245          250          255
Cys Gly Gly Val Leu Val His Pro Gln Trp Val Leu Thr Ala Ala His
          260          265          270
Cys Ile Arg Asn Lys Ser Val Ile Leu Leu Gly Arg His Ser Leu Phe
          275          280          285
His Pro Glu Asp Thr Gly Gln Val Phe Gln Val Ser His Ser Phe Pro
          290          295          300
His Pro Leu Tyr Asp Met Ser Leu Leu Lys Asn Arg Phe Leu Arg Pro
          305          310          315          320
Gly Asp Asp Ser Ser His Asp Leu Met Leu Leu Arg Leu Ser Glu Pro
          325          330          335
Ala Glu Leu Thr Asp Ala Val Lys Val Met Asp Leu Pro Thr Gln Glu
          340          345          350
Pro Ala Leu Gly Thr Thr Cys Tyr Ala Ser Gly Trp Gly Ser Ile Glu
          355          360          365
Pro Glu Glu Phe Leu Thr Pro Lys Lys Leu Gln Cys Val Asp Leu His
          370          375          380
Val Ile Ser Asn Asp Val Cys Ala Gln Val His Pro Gln Lys Val Thr
          385          390          395          400

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<210> 618
<211> 385
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(385)
<223> n = A,T,C or G
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<400>	618						
ctgtgctgag	aaccaaaagc	tatgancact	gcttttccaa	atgtccataa	naccaacatt		60
ttttactacta	ccaccactac	ctgggagctc	nttagaaagc	tagtctcccg	ggcaccaccc		120
tggcctactc	aacctaatgt	gcatttaaca	agattnacgt	ngaaatctgc	aaagcacagg		180
ggcngataac	agtaccacct	gntctgggtc	ctanccccc	gacccttaca	gtctaactgg		240
gacacaagg	cttnaaatca	aattgcctat	cattaagata	tacaanganc	ntgagaaact		300
gctnacttta	tntattaagg	ngctctaaga	cttagaaacn	aaangcantg	ctgagangat		360
tcaaatatga	ngggggncac	tttnc					380

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<210> 619
<211> 869
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(869)
<223> n = A,T,C or G
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<400>	619						
gatatcccg	gaattcgcg	cgcgctcgac	ctctacttgt	ttagacataa	atgcagtc		60
gcattaaaga	tcctttaaaa	aaatgtttt	ccaatggtta	aaagacaagc	tcaaataaat		120
gaactctcat	acatatgcc	aaatgatga	gtagattaaat	atttcagtag	gtagttacta		180
gctttctgtg	tatgagtaaa	catatgggag	aaatataaaa	cactaaagta	gactcaatga		240
aagcatagta	tcctatgtat	tcgtttttc	gaaatgtcta	atgaagggaag	gaaacaatga		300
atgaatgcc	tattctctct	tagagtgtct	ggacatggtt	tgtcgctgaa	acttcattgt		360
aaatttatat	tittgctac	attacgccca	tcttagacct	atacgtataa	gacataaggc		420
atatcttatg	tcttacatgt	ataataatct	aagcagaaca	aaaaataaac	aaatattttc		480
tccccaaat	ttttgagaca	ggtgatttt	cgggaagat	gtgtttaagct	tttaatcctg		540
tgggtttgtg	taccacactg	cacactagag	tgttgctcta	attcagtgag	tgttaactct		600
gggtgaacag	tggaaatact	agggtacatt	ttaaaaatgc	taatgctcgg	ctctcgctga		660
agaccaaatt	aattggaatc	tctgnngng	gnattgatct	ttttataatc	tttotanang		720
attctaatgg	gcttcagggt	atgaaaacn	ctgntggagc	tnggaacctt	cctttagttt		780
ggagaaccc	cgatgaggt	ntnttaggcn	cgcctnttt	ttggcctggg	cttcccctct		840
tatntnttt	tgggaangnc	cnaaatttt					860

<210>	620
<211>	339
<212>	DNA

220

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(339)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 620

gngcgggcct	cncctgtgctt	gctctcgtctg	ccgacgctct	ttttccacca	gctgtaggan	60
aagcccgaag	accactgggc	ccccgggtag	cccaagtacc	actggtcctc	ctggctcctg	120
acgctnccgg	tcttctcgt	ggcgtagact	gccagcttcg	gagaccctc	agccctccc	180
cgcttttctc	caccccagga	ggccatcagt	agcgagctac	tgcttcggcc	acaacctccc	240
agcangatag	cccgcggttt	ccaatctgcg	aaaggaggac	cgccnagccc	gaaatgccna	300
gcccagcnat	cactgccacg	ccgagccnag	cgctcgtgc			339

&lt;210&gt; 621

&lt;211&gt; 267

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(267)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 621

ggggngcatg	gtcccnngta	gccaagtaca	tggtcctcct	ggctcctgac	gctacgggtc	60
ttcctcgttg	cgtagactgc	cagcttcgga	gacccctcag	cccctccccg	cttttctcca	120
ccccaggagg	ccatcagtag	cgagctactg	cctcgccac	aacctccag	caggatngcc	180
cgcggtttcc	aatctgcaa	aggaggaccg	ccnagccaga	aatgccnagc	cnagcgatca	240
ctgccacgcc	nagccnagcg	ctcgtgc				267

&lt;210&gt; 622

&lt;211&gt; 847

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(847)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 622

cttangntgt	cgactgacgt	catgcatgan	ttaaagcaga	ggtttggtga	aatttatgaa	60
aaatacaaaa	ttccggcttg	tcctgaggaa	gagccactac	ttgataactc	tacaagagga	120
acagatgtga	aggatattcc	ctttaatttg	acaaataaca	tacctggttg	tgaggaagaa	180
gatgcatctg	aaatatctgt	ctcagtggta	ttcgagacat	ttcctgaaca	aaaagaaccc	240
agtctcaaaa	atatcatcca	tccatactat	catccgtact	ctgggtccca	ggaacatgtt	300
tgccagtc	cttctaagct	tcattttacat	gaaaataaat	tagactgcga	caatgataac	360
aaactaggca	ttggacatat	ttttagtaca	gataacaact	ttcataatga	tgcaagcact	420
aagaaagcaa	ggaacccaga	agtggttacg	gttgaaatga	aagaagacca	agagtttgat	480
ttgcaaatga	caaaaaatat	gaacccaaat	agtgcagtg	gcagtacaaa	taactataaa	540
agcctgaaac	ctaaaattaga	aaatctgagt	tctttaccac	cagattctga	cagaacatca	600
ggaagtatat	ctacatgaag	aattacagca	agacatgcc	aaagttaaag	aatgangtca	660
acacattaga	aanaagantt	ctgggctttg	aagaaagaaa	atgttccact	tcataaagaa	720
ggttgaaaga	agaatgggag	agcccngaan	tttttgcccn	gaaattttcg	ggaaccctac	780
tgatgggtc	nactggttg	ccatgaatga	ataatggact	aatcnccaa	ttcctnggga	840
agggaat						847

221

<210> 623  
<211> 681  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(681)  
<223> n = A,T,C or G

<400> 623  
aaaactgtac tcgcgcgctg catgtcgaca ctagtggatc caaagaatcg gcacgagcga 60  
aaangctcan gcagcccggc tggccgccgc cgctcctccc cccaggaaaag ccaangtgga 120  
ngctgatgtg gctgcangag ctcgtttcac agccctcan gtgganctgg ttgggccgag 180  
gctgccangg gcggaagtgg gtgtccccc gtctcagccc caaggctgcc cctcacaag 240  
cactggtggt ttgcctccac tgccaccttg ggctccgaac ccgctccct gctgtggang 300  
cccaccgtgg gaatccaggt ccccagggtg actgcctgcc ttgccctcac tgcccactct 360  
gcccacactt ccctgcctag anaccgggaa ggggctgtgt cggtantggt gcccacctgg 420  
atgtggcagc accgactgtg ggggtggacc tggccttgcc ggggtcaaaa gtgggggccc 480  
ngggaaaagc acctgaagtg gccctgaaaa atccccctt aattttccc caatttggg 540  
ctcnaacaaa aggaaattgc tgaagccaan ggtaccaagg tcaccctaa ggccagggtg 600  
aaaaggtccc aaaattccaa tnccacccnt ttgggcttnc ctcttggaac cccggcccc 660  
tctcntgaan ttttaaaaaa n 681

<210> 624  
<211> 661  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(661)  
<223> n = A,T,C or G

<400> 624  
attggtctta ctgtaccacc gggtggaat cgatggccgc ggcgtctaaa tatccgattt 60  
ttttttttt tctctttctg actgtccatg gacaaatgaa actaacttaa tctaactaaa 120  
aaacacaact atattttgaa gattttctat ctgcaactca ggacactttc cacncggttg 180  
ttgttacctt ttggtcttgt ctctgaacat gaaattnatc tcaagggatt ngatttctgg 240  
acctcctatt cctgctatgg gtttgatatt tcttgggctc cagggccact gttgcattgg 300  
gntgacagnt acctoctagc ccatancctc ctatcttggg aaacaaacct aacaactacg 360  
tgtaccttcc atagatctct gattgagtct cagtatnccg ttgctcatgg gcgattcact 420  
tgaatccgtn attggtgcca acaatctga ctcatgggnn aatggatcct atcacgttcc 480  
cctgattngc aaccctgta tacatanatc taatcgcata gaatctagcn tnggntatgc 540  
gcggctacgc tatcagggtg tgntaactat ngcatggcta cgaancctga tcatgatcna 600  
gggtcatgga ctcttatcag gggggttggg ccgngcttct ttttcnnacc ttggtaaaaa 660  
c 661

<210> 625  
<211> 181  
<212> DNA  
<213> Homo sapien

<400> 625  
gcaacaatca gatcatgtta aagtaaactc ccattgccct ggatcacttc aggatttaat 60  
tgtccaagga gagcagggtt ctctgtgtaa aaaaagggtg ggaatgttt gagagtaaaa 120  
aatacaaaaat tcaaccggtc gaaaatacac cactccattc agtgccttac ccccataagc 180

222

c 181

<210> 626  
 <211> 181  
 <212> DNA  
 <213> Homo sapien

<400> 626  
 gcaacaatca gatcatgtta aagtaaatct ccattgccct ggatcacttc aggatttaat 60  
 tgtccaagga gagcagggtt ctctgtgaa aaaaagggtg ggaaatgttt gagagtaaaa 120  
 aatacaaaat tcaaccggtc gaaaatacac cactccattc agtgctctac ccccataagc 180  
 c 181

<210> 627  
 <211> 813  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(813)  
 <223> n = A,T,C or G

<400> 627  
 accaagctgg agctcgcgcg cctgcaggtc gacactagtg gatccaaagt gaacgtgaag 60  
 gtgagcagag gagaacttgc gatggcaaag ttaaaaacaa gaggagatga tggctcttgt 120  
 gtggcacagg atgttataaaa aattctcctg tccttaagga gttactgcta tttgagtaat 180  
 gtgccacttc cctacatagc cttctatgca gaaatgctat atttccactt cacaacccag 240  
 aacgtgcatt ttattttaca tttagaggag gaacaaacaa ccagaaggca aaaactggtg 300  
 cattattttt tgcaattctc ttggaaaagag ttcgttttta acttctgctc agacagcaca 360  
 caactactgg gaatatattt taatttcaaa tctgatgtgt gacatctggt aactcattta 420  
 ttgctaataa agttttcaca ggaagcagca gtcaccagta gctcatctta tttttcagtt 480  
 ggcaaagtgt tgtttacott ttattggcct gcacgcgtgt ctcttatcac aggatattta 540  
 attagaaaac gcaagtagcc taacatagaa nagaaatgga gtggtagata atagtagata 600  
 gaatggctaa atatttttat tacagtgatg taatatcact gnaatttatg gttaaaaatt 660  
 atgtaatact caaaagggaat tctcagactg gcgaaacagc tggncacagc ctntcacagg 720  
 gctttnanct cctnttgagc tttcccccgt ntggacttta gtcttccttt tacncccgna 780  
 gtnccattn nttaccaatt gtnccgggaa ana 813

<210> 628  
 <211> 646  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(646)  
 <223> n = A,T,C or G

<400> 628  
 tttggngngn ggtgtctent ttgggtggac tttttgggtc gtagggcccc aaggccgtta 60  
 atcccgtaat aacggaagac gaagaagagt cagaagagtg cttctataag gatcgggacg 120  
 agactacott agaggataaa aggaaaaaag cagaggagga agagtggtag aaggagtcag 180  
 aagaacacca cacgtcgttc tgaacctgga gccttatcaa aaaggtctag ataaacgata 240  
 gcgatctcga tatcgagctc aagaggtagg tttagagact tctcgtcctc gagagcgaaa 300  
 tggaaagatc cgacgacgat aagaagttaa agtgtagagg gtgcttgagg agcgcgtgga 360  
 aggattctgc ggaggggacc atcgacgtag agacttgaag gcctactaag gtccacaaga 420  
 agcccggctc tttctccgaa tggtcggagc gtacagtatg cgacgtcgat cggcagacaa 480

223

```

gctggcggtta gactcgaagt gttcggggcga atcgacttat aatagtcgcg cgctagtaac 540
gtaggaaacac gaagagtagt cgaaagaaaa cgtttagtga gggaaaagat tagggaaaaa 600
ggagaggcctt aataactaag acacttggag cctaggccaa cgcgaa 646

```

&lt;210&gt; 629

&lt;211&gt; 617

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(617)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 629

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gccccncccc ccctcctngg gcttatnggg acagaccac gtagtactct aaatcttctc 60
ctacgcggga caacggaccc tataccaatt cgaatcttgg aactccgac cgccggattc 120
tcttccccctt tcggcttccc ctttctgtcg gtaccctcc ctagtcgtct cctacacctt 180
cgtaccgtcg atatatagtc gccgcggact agcctattta ggtgtcctag actcgttatt 240
gatccactca ttagtctagt actatgcgtc acgtatctta gttgcctaag agggagatta 300
aatcctccac aagttccgac gaattcctgg actctcgta tagcaaacct tcttatgagg 360
cttcttgta tatcttctgg atgtttctcg tgtcccggtc ctccgctact actagagctc 420
cttgccctat ctctagaagt agaggactct cgggttcggt ctccaaatct agcgctagag 480
ctatcgctac ccgctcgatt cccccagcgg aatcttgaaa cctgaggtag tacacaaacc 540
ctcncatct tccctcggtt gctccttctt ctcaccccc cttcccgctt tctcggaan 600
gaatctactt tancttc 617

```

&lt;210&gt; 630

&lt;211&gt; 644

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(644)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 630

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cnntcggcnt gggtttntt ctgagnnnc ccccccccc cccccccaa cttacacca 60
ccaaacactt tccgccccct acctaggaga cattagaagg gtttaggctt cggcgatatag 120
taaagtcctc tacctcggaa gtagagaatt cggtagttta attcagggtt agaggctcgc 180
tcgttagatt tatagtttag gtttagaatc ggaaaccttc gatcttcctt agaagggtaa 240
taagtgaggc cctaaatccg tctaaccaag gcgttaaggc ccgtacctaa acctagtctt 300
atcttctatc aggcgcacca atataggtag gttctacttt cgtataggcc ttaagggaata 360
gttcggtagt tatcgaaggc actcctctct aggcctaggct tttctcagtc ttagtactcc 420
gggaccgtcg tcgcanaaat atcgatggac ggtaggtatc tccgcgttac gcgtcgggct 480
agggatatag agcgaattat cggcgagagg cggtcgctan gaatcgggat caatatgntg 540
ttctttaccc tacggatatc ggagaaaaac ataaaacctt ctnaccangg ataagggtatt 600
atcggacccc taaaataaca gtaacattta gantactagt accc 644

```

&lt;210&gt; 631

&lt;211&gt; 526

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(526)



<223> n = A,T,C or G

<400> 631

ccntcggctt	gggttttttt	ctgagccccc	ccccccccc	ccccccccc	cccccccggc	60
cccatagccc	caccggnccc	acccaaattt	taacaaaata	aatntaccta	tcgntcacct	120
atcccnegta	tcgngtaggt	cggtagccgt	accgngatc	ncnacgattn	ttcgggtcgt	180
cncccttaan	acggncccg	agccnccgga	anaaatacta	cgagngactc	taatntagca	240
anaccgcgcg	tcnattanta	gcaccccttag	tcttccaatg	ncgnggattn	ngaatacctn	300
naagtattcg	ggtagaacgg	gtcccgggtc	cccgcctct	ttncatataa	cgccgggtac	360
aaantcgggt	tctaaattcc	ncacgaattt	ngncggcaac	attcncgggn	ccttattanc	420
cntttccaac	cccataacnc	nagctcgatc	gggctttanc	gaatccgggg	tcncccccca	480
ngantccggg	tcctttgagt	ngctctagga	cggttacgac	ggagga		526

<210> 632

<211> 647

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(647)

<223> n = A,T,C or G

<400> 632

tttggngggc	ggngctcat	ttgggtggac	tttttgggtc	gtaggaacct	ggtatgagg	60
gtgttttgta	tttctcttc	gtcgtctctg	ggaggttcgg	tttcgattga	gattcgggtt	120
cgtctttatc	ttacgaggca	ccctgatatt	gttgccgttt	ggtttggttg	tggagagttt	180
tgtcctactc	tagcgggtca	tgccgatgat	atgtagcctg	cgtggcctga	tagtgatgtt	240
gtgagcttga	gaggggagtt	gtgggtgttg	cgggcggagt	aggaggggtt	ggagcaccgg	300
gattgggaga	tatagaatca	taagtgttag	gtatagggtc	attgagcgag	ttcgtggaat	360
tcgtgtggtc	atcataatta	gagtgggat	gggctctata	tttcttagag	gacgcacggt	420
cgtgattcgg	ggtttgatgg	gtgttctct	tgtgggcacg	attagcttgt	tcatgatggt	480
aaggaccata	ctgtttcgaa	tgaggattcg	tgtcttcgga	ttgttggtga	tattgtggnc	540
tanactattt	agtgttaagc	ggaggtggtt	tgccgtggtg	gagtatccga	nnttcattcg	600
ganggtatgc	gtgcggagcg	gtccttgtag	acattccgga	aaaatgg		647

<210> 633

<211> 630

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(630)

<223> n = A,T,C or G

<400> 633

tccttcgggt	tggttttttt	tctgaacccc	ccccccccc	ccccctcgga	aggcctctag	60
gtcccccacc	gtctctctaa	tcctcaggaa	ccgatccacc	caaccaactt	actaatgtcc	120
tacagtaaac	acccgagaat	ataaaccac	acctaggcct	ccaatcctac	cagggaagca	180
agaagccgta	gtctagcgta	ttacgaaccc	gagatagaga	cggagatact	tagttttatt	240
ctctcgggaat	aggaaagacg	actggggagg	gaatataggc	tagcgcgggg	ataggggcta	300
tgccggatat	gggggcgggt	cgctctctta	ttctcttata	ccacgtcaat	aggaatgtag	360
atatacctag	atgttcccgt	agaaagagac	gttagagggtc	tccgaagcta	taaaggagag	420
gcgcgaagaa	acttcgtact	ctagctttat	ataggttagtc	gctctagtcc	cataagcgac	480
gagagatcta	ctagatttcg	gtatcgccgt	cgatatgtatt	cgaatatagtc	ttcttcccct	540
tttcgatctc	ctctctatac	tacatggnga	ttatagtcnt	aagatagtc	ggatatttag	600
atattagtta	tatgacgttc	gacgggacgg				630

225

<210> 634  
<211> 647  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(647)  
<223> n = A,T,C or G

<400> 634  
ccntcggcctt ggggttttttt ctgacccccc cccccccccc cctccactaa gancttaacc 60  
caaccctata gtttactcgt atagggggaat cgaggagaaa taggaacgaa gagcgggtga 120  
taaagagaaa gtactttcct ttatatgtta agagcttagc gtaatgactt tcgttatatg 180  
gctagttagt tttatccggc gttatagggc ttagttctgg ttatctcggg tctaattccc 240  
ttagtatgct cgggagttaa acgaggtcac gggatagcgc gtaccctttc taaggttcct 300  
ggaaaagctat tcgttatatta tcgcgattct cgaggtcgaa aggatcaagg atcttccctt 360  
ttactaccct agtcgggtta gcggtcggtc aaaactagtg tagtacctt acctcctoga 420  
aagttatagt cgaacaacg tattagtcga aattatagcg gatagatcga gacggttctt 480  
tctcgggttc tcagccggta atccctctat ttgggggtct tctccctctt ccccttgtc 540  
ttcgcctta gcttccaagg ttctcggaa gcgaggggtt ctacttaagt cgntagcgtt 600  
ccttataaac cncctacag cagacccct tgtaaacggc tcggggt 647

<210> 635  
<211> 645  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(645)  
<223> n = A,T,C or G

<400> 635  
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ataaaagact tcgcgcgggt agctacacag cctacgggaa tctcacgaat cccgattcaa 180  
gtcccactct cgaccacacc ccggtatcgt cgttttccca taccaatgtc gaaaaataaa 240  
ataaaatcca gtcaagcccc acggttaagcg ggggtagggc taggcgaaga ggcaggaacc 300  
gttcgaggcc gggggtttt aaaaatacaa acaactactt aaagtattacc ccttctaaag 360  
tcgggggcaa cggttaaagc acgcctctaa agtactactc gtttcgagaa ggggtagtca 420  
tctcccgcac agagactctc gcgtatatca actcgcacgc cttctagcat tccgacggtc 480  
gcccgcggtt acatatcttg cggattagct ccgagggact atagggttaa ttagtctagt 540  
aaattctctt agaggatagt cggggtcgta gttaggcagt acgaggggac atgggctgctg 600  
tcgtgctcta ccttgacagc atactcttat aaacatcttt ttcct 645

<210> 636  
<211> 643  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(643)  
<223> n = A,T,C or G

<400> 636

226

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ccttcggcctt gggttttttt ctgacccccc cccccccccc cctagcgga aacaatcccc 60
accgagatttt tattaatcgt aaaactcgcc ttcggtacca agtcttcctc cttcccgtaa 120
cctggctccc tctagnngc tttacgaacg tccctcctct tcttacggct cggaagtgggt 180
tacggttaaa tccggaggng gggctaacga atccaaggct aactcctctt anagtttggt 240
gtcncncngt ttagtaagga tccgtggagg gcgagtattt gncccccggc ctttatnta 300
tagttoccta gtacgataaa gntaccggct atcctattac agcggataaa agttatttan 360
agggccgacg tcnccgctag acaggctaca gctagnggag gtaccgcctc cgactantcc 420
gttgnttcgg acaaggngt ttcggttaac tccacaaact cctccgccga ctctanggtg 480
gggacggcag ttccncngt tagtgtgctg tatagagaag ggcatttgag ttggacgtta 540
cnttttaaca taggttattc cgtttaggtt cttgcgggcc cgtgggggta gtncnccggc 600
gcgttnttat cggcgatttt ccgcagtttc cgtttccggn tnt 643

```

&lt;210&gt; 637

&lt;211&gt; 631

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(631)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 637

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gggttntctc atttgggtgg actttttggg tcgtaggaac cggtatgnag gagtaggagt 60
cgctgggaag actagaagtt agctacggac gattagtgtg attccactct taataacgag 120
taatcgttta cgtcgggttg gtgtttcggg gttttggaga gtaagcgtag ttgtggagtt 180
tcgcatatag gtccctttac ttccggcgtc tcgtcttctg tcggttaggt tattattggt 240
catccttcgc attagtagta gggttggtcg gataaatcga tagctattct ttagaattcg 300
tagtcggaga attcgtgtac gaagtccttt aagttcttta agttcgcgag taagacgtgt 360
acggttattt tgcgtcgcac gttagtgtcg tttacgggag ttctgtttta ggggtttacg 420
tagaacgtta ttaagcacgg taatacgata gaggattacg cgacgtattc gtcttagaac 480
gtcgtatttt cgaaggcgca tttgttatcg aaggggagtc cttggagaat cgagatattc 540
caagaatatt acggagatta cagatcgga ggctcccag atcggacgta ttaccggtct 600
cgcccgaaac gagtaggtat cntccgata a 631

```

&lt;210&gt; 638

&lt;211&gt; 606

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(606)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 638

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ccccccccc ctcaaccatc nattccccac ctcaacgcga attacggttt cgaaagtcga 60
caataagtcc ggtcgagtag agggaatcag gggctggtan aaaggaccac gggcggaaaa 120
taccggtctc cttccgggga gcgacgtcgg ggaaaggga gagagcggtc tagttcgtag 180
gcaaacaggt cagaaaagtt aaggttaaag gtcggagggg agaggatagc tagtacgctt 240
agttcggggc tcgggcgcag ggccactttc ctctttcgcg ttccctttact ctgcttacga 300
gttcaggctc cggagttccg cgccggagggt cgtcgcgacg ctaggaatgg ggactcgctc 360
agtccccggt tatccttcgg gattctatgt tttcgccgat agacggagac cgggtagtag 420
ggttccgctg taccgccact cgtcgccttg atccggcccg ctccgcttaa gggcgatgaa 480
agattaggtt ttagggctct acgggacgag gcatagggcg ggagaagggg ggaggggtcg 540
ggggtcgaag ggantaagaa atcgcantcg cgcggggctg gtagganccg aaatttttct 600
cnncgt 606

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227

<210> 639  
<211> 592  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(592)  
<223> n = A,T,C or G

<400> 639  
tccntcggct tgggtttttt totgagcccc cccccccccc cccccgggaa cgagaaaaca 60  
atcccaccct accgcgggga gtgggttgna cgcttagttc tagaatcctc ggaatcgtcc 120  
tccggcggtg gtagttccgg cgattccgag tatgccgaag tgtatcgctc cgtctagagg 180  
ttggtatctg tttatcgga tgacgctatt gactcggatg ctttcgaagt agggggatag 240  
gcgcatagat acgcctccgc ggtgtcctct gaagtggccg catccgtgga cgcagcgtag 300  
acagctctgg tggacgataa cggcttctcg tactcctact ccggctatta tgtagagag 360  
gacttgtttc tgaacggata taccattagc gaaggggtac cctccgctaa cgcaggcggt 420  
tctaacagtt cttccgggcg ctccgaattt agattgaagc ctccgcagca ttgtgggatc 480  
ctcttcggtt agccctcttt ataggatttc tctccgccc cgaaagangg ctggtcgtcc 540  
ccggcangta tgtctagctc gaacgcttg ttactccttt gttttcgaaa na 592

<210> 640  
<211> 637  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(637)  
<223> n = A,T,C or G

<400> 640  
ctttgtggcg gtggnlgtct catttgggtg gacttttttg gtcgtaggct tatccgggtn 60  
gggctcccgga agtagcttag gatcgccggc tagttccggt cccgcccgtc gaaagcgcg 120  
ttcggcgggc ggcccccgct tcgttcgagg gctttaccct catagagtgc caggctctcg 180  
ttcttacggg ttctgcggcg atagatttta cggcgagagg tcggtatctt cgccgcttta 240  
cgttcggtcg gcatctacgc ctagtccaca ggtagtttat gcgccggagc gcgtgacgga 300  
gaggttatag gggacgcgga agaaccgcct ccaaatgact agtacaggct cgttcgggcg 360  
tagatctcct cgctcggtcg gcggttctta cttctagggc cgctctacgg tttaaggcgg 420  
tcgttagatc ttagaaacta tactcaagtt tcagtcggaa gaaaggaggt agagagaagg 480  
gtaaacgatt acctccggtt ctagcccttt ttactcgcat aacgggagaa cggggtcgg 540  
ctctcagata cgcctcgga gacgtcgga ttcaacttta acctccgcta gggcatccgt 600  
atacggttaa cgcggtaaaa gcgacctcg aaacctc 637

<210> 641  
<211> 649  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(649)  
<223> n = A,T,C or G

<400> 641  
ctntgtggcg gtggttgtct cagtttgggt ggatttttg gtcgtaggna acctggtatg 60  
aggtctagtt tcttcaacga ttcttggttc agttacgga ccctatcctt atcttacaat 120

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gtctttctaca tcaggttcat caattaatat atcaattaca cattaacgac ggtgtgacgc 180
aatatgagaa agtatacatt aaggttatta tatattattc gcttaaaaag gttcctgaca 240
tgggacaact tcaccaccca ttctagaagc ccccccctct gtaggacccc ctcgagttcc 300
ccattatctt agttcagttt tcatttttta accaggaggg tatcggtttt taataggtag 360
tattttgtca aacttttcag aagctttatc ttcaaataata cttgcaccat ctgtactagg 420
agcactaact attcgagtct attacagctc aacagaaaat aattgaaatt aaacaacctc 480
agtatcgctc accataaccc catcgggctc tcacccattc tottcataag ttctagagca 540
tcctgagctc tttcctatta cccttgatgg tactcatggg ctaatacccc ccgcagttat 600
aggtccttat ggatcctatg ctaccaccgg tctaatacct tctatcacn 649

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&lt;210&gt; 642

&lt;211&gt; 645

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(645)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 642

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tccttcggct tgggtttttt ttcgtcgagg gttactatta tcgattgtta cttgtaaagg 60
cgatactccc accgctcacg atattagacc tgctcctcta gaagcgaacg gcgataggtc 120
tactcggccg gcgaagacgg cgaacgggta ggaggagcca tatgcaaccc taacggagat 180
tataagtact gggaaaaata ctagtattaa ggtagcgggt taagataggt ggagagacac 240
tattcacgag cataagcact tagaaggctt tctcgaggag aggtaggcta cggactacgt 300
tccttcttcc tctagcctcg agaggagtag tagatgatte gcaaaagaga atccctccta 360
tacgctggca taactagacg acgctgcgtc gggaaatctc gccaaccccta ttgcgacctc 420
caaaaaggaa attgtcggtt catagaacgc taataactccg ggtcttcccg aatcatagcc 480
gcataatcgg aagaagacgg taaaatcgcg cgattctaac aagattctgt agacttaagg 540
ctaagcacta gaagcgatct cgattccgga tcttaagatc atactaatag ttcggtcaca 600
ccagacgacg attagccact agaagcccta ctccgtngaa accgg 645

```

&lt;210&gt; 643

&lt;211&gt; 586

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(586)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 643

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ctttgtggcg gcggtgtctc atttgggtgg atttttgggt cgtaggaacc tggtagcag 60
ggtccgcccg gaattaaaag cgggatcccc aaaacgmnngn ttcgcaagaa gagaagaatc 120
atagcgatag anctttcata gtacaaaggt aactaagagg aaaataatgc agattcagaa 180
ctagttgccg aattagaact cgattaggcc aaggatccga gcctggcgct atcacttcgg 240
gacttaagct acggtagagc agtcggtcct gaagcatagc tcccgtagga cgtaggaaac 300
tagtccggca cggaggacat actctcgagt ctcggaacgt ctatttagaa tataaacgca 360
ttaacctcag aaggcgccga cgcggttact ctctagggaa ctatttcatt ccttcggag 420
ctcccctatt tttccaacac atataccggc aaaggaaaat cttntgtcct cgggtctaaag 480
agagggaaaa aaaacgatat ctagggtcgg gtttatccat ttaaaaanat ngacgcgact 540
actccctttc aaaggaggtt tccccctagg nagagttcaa cngaag 586

```

&lt;210&gt; 644

&lt;211&gt; 646

&lt;212&gt; DNA

229

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(646)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 644

ctttgtggcg	gtggttgtct	catttgggtg	gcatttttgg	gtcgtaggaa	cctggtatng	60
agggctatnt	gacttgtttc	tcaaattccca	tggtatgggtg	gggtggcgtgc	ggggtggcgg	120
tcggttcggc	gggggtgggg	gtcgtcctcc	aaaggagtgg	ctagagggtct	tttagtgggt	180
ttaggggcgg	aagggttag	agcggagaga	cgctgcgtg	gaagcttctg	gcggagcgcg	240
agaaggtagt	tagcgcgggt	tcggaagatt	ctcagaattc	gagaagaggt	agtggggcgc	300
ggagagagag	tttctaagtc	taaacgtaga	ggctgcctca	gtcgggccgg	gagtagcttt	360
taagctagag	gtcagggtcc	tcgttttaggc	tcggggctct	tcgggcagta	tcctctttct	420
cgaggaaacg	agcgaccgac	gtcgtagccg	gacccgtota	tcggtacgtt	tagagatacg	480
ctcacctcca	cgggcgtata	tgcccgata	cgtataaacg	cgtaataatac	tcgcgcgtaa	540
aacacgtata	cactatatac	acgcacgtg	cggaccgtat	agcgttatac	gcgcgcgtat	600
attaatttac	acttatatac	gcgttaaac	gatataatc	acnccg		646

&lt;210&gt; 645

&lt;211&gt; 654

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(654)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 645

ncnctcggt	tggtttttt	tctgacccc	ccccccccc	cccccggtcg	acaacgtgcc	60
caccgttgcc	atcccagcat	agctgggtcg	ttctgtttta	ttcttagtag	tttagttcgc	120
ctatagtccc	tcgtctatcg	tctatcattt	aaggaggcgg	ggctcgtctt	ttaggcgggg	180
tatcttaggt	attcttctg	tttcgggtgc	cgtctcggag	tctggtcctt	ttgctttcct	240
ttcttggtcg	aacttcgtgt	ttgatcgcgt	tggtttctttg	gggtcgtcat	acctaagggc	300
cacttcgcca	acaacaagt	ttgtgtagtc	gtttctatta	gggttcgctg	gccggcgctc	360
ttactgggtg	gcgattttta	acgcgttttg	ttttaatttg	cttcctcccc	tagggctcgc	420
tcggtcttct	ctctgttcgc	tgctctcgtc	cggccttttg	tcgggggata	gctccggcta	480
ttancgtgcc	gtgtccgtgt	ggntttttgc	caatgtgaag	gcctaggggt	gcgggcttct	540
ttggccatgg	nttcccctct	tgtgancctt	aggggtaacg	antcgttaatt	naaggtcggg	600
ggttggnata	cgttntangg	gangcctgng	tcgntattc	cttgttttgg	cctn	654

&lt;210&gt; 646

&lt;211&gt; 645

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(645)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 646

tccttcgggt	tggtttttt	tctgagcccc	ccccccccc	ccccacggcc	aagtacacag	60
accacacaaa	aacaacgtca	acacaacttc	gggtatacgg	accttaagag	agaccccgtg	120
gtagacccta	ccacagccat	ccaatagtca	aacaacaagg	gcgcacccaa	tccatccata	180
gagctatcaa	acaacggagg	ggaaaggaaa	gagcagggtc	aacttagcag	agatcgaagt	240

cggcactaat	tcctttcaag	tactcgctcg	gctttagt	cggggtaaag	tccgctctca	300
aaggggccaac	gaggttttaa	agcgaccccc	gtatcgagtc	ttcttcgtat	tcattaaggc	360
gttaaaggta	cgagacctag	aagagagtag	aattagccca	ccaaatcgcc	taaaccggca	420
aaaacgacca	aaagtcaaaag	acccttaca	atatcacctt	aaaacgcca	ccccaaaaac	480
gcgatcagta	acgcacgtac	ctttcccacg	cttttctttc	tttactctc	caaaacaaac	540
ccgaatattt	agcgcaaaaa	atatccgagg	gagaattaga	agctattacc	cgaaaaaaa	600
ncgganangg	antaaatngt	ggggaatana	cgtttggtt	ttctg		645

&lt;210&gt; 647

&lt;211&gt; 753

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(753)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 647

accttacctg	gtaccgggccc	ccccctcgag	ttttttttt	tccaaataca	actcagattg	60
tatacgaaaa	gctgataata	cattgacttt	tgtgttttaa	atcccttgag	cctttgataa	120
tgattttttt	tgtgttaaca	attgtagtat	ataaaatcgg	attcaccatc	cttctgatgc	180
catattgatt	agtttgattt	tatggtgatg	ggatcattgt	gtgttaactg	tattaagaag	240
aaatggattt	gattgacttt	gcacccattt	ttatctgtgt	tactttcatg	ttttatttaa	300
aagcattttc	ggaccagaat	aagttaagtg	gtataatttg	ctttttacac	gtttatataa	360
ttgaagttag	caatgtggca	aaatctctaa	tggaaataaa	atgcttcaga	atgatgacat	420
aaatctgagc	tatttcttgc	ctggagaaca	agtgttattc	ataataattt	aatagcttct	480
gaggtgtttt	gttcattgtg	tgaaggctta	tccacctgtg	atcaattcat	gggctctgct	540
ttgtttaatg	tagtcagggt	gttaatacna	gacttaagag	tcdtcctact	gtgataagtg	600
gtgagtgaag	attacatgtc	ttangaaaa	tatactggga	atatctctga	cattaatggg	660
tttaaatgtt	ttaaggctag	gggatgatgc	aatgganaan	atncttccaa	angtttctgg	720
ttgtttatat	ttgnggaagn	catnaagana	ccg			753

&lt;210&gt; 648

&lt;211&gt; 383

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(383)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 648

gatatcccg	ggaaatgcg	aggcctttng	gcttacgtgt	ttaccgcgta	gggcaaagcc	60
ttgncaaatt	cccggccagc	ggagcggcga	gggtggggac	tcacgggaag	ttaaacagcc	120
tcgtcggcgt	cctcgaggct	ccaaaaccag	gctctaggcg	gggacgactg	cagccgttat	180
ggaggccacc	gcggctacg	ccgcggctga	ggcctcccca	ggtggagcgg	tggcctggag	240
gggaatcttg	atcctgggccc	agccacctgt	caagaggagg	cggagcgtca	tgcctctgga	300
agactggatg	aattattctc	aggagcctga	cgaaggcgaa	gaagtctttg	cagaggaaat	360
tgaatgctgt	ctgatgctac	aat				383

&lt;210&gt; 649

&lt;211&gt; 349

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

<221> misc\_feature  
 <222> (1)...(349)  
 <223> n = A,T,C or G

<400> 649  
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 cagtgtgggt ggaattccat tgtgttgggt cactagttaa tggatttagc tagacanagg 120  
 anatttacc tttccattt agcacagtga gganaggcta nacagctagg atgcaataaa 180  
 aaaaatttta atgagaaatg tgtgtggttag attaatctta ttaatctcaa gttatagatt 240  
 aaaaatttta agtaccncat aaatgccatt tgcctttgct aangntacat ttttatgaan 300  
 aangaccntg catacnaat ganatactgg actttnggna cttgangga 349

<210> 650  
 <211> 306  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(306)  
 <223> n = A,T,C or G

<400> 650  
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 aatccccaaa tatatcatat tgacatgaat atatcatctc ctcaatgtcc agcattagca 120  
 gacaagatga gtgctgaaga tgatataact cctacctctt atgtaggcta gaggtaaagt 180  
 ctggtctctg tgactgtggg gacataccga aaaggaatgt gggttaatat cagangacct 240  
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 tgaacc 306

<210> 651  
 <211> 769  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(769)  
 <223> n = A,T,C or G

<400> 651  
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 catgtcttag aagcactctg gttgttgcta ggcagacaat tttacatctc ttgctatacc 120  
 agttgcatga agttcatcat gcatattggc tgtggaaaac ctttaacagca tcatgtcata 180  
 aggtttcagt aaggtttaaa tgaaatcatg tattaagcac ttagtatagt gcaccttaaa 240  
 tgttagcttc aaaacaatga caacctaaact aatgttgaaa gaagcttggt tttgtaaatt 300  
 atgtcttatt gaaagatgtc atcaaatcct gttatttcta atcccttaaa gtctctcaat 360  
 gtattttctt ttgccatctc caatgacagg accttagttt aagccagtggt ttctctcaac 420  
 ttctaatacca gagatacctg ggtgtcccca agaccttttc agagcatcct tgatgtcaaa 480  
 accattttca taataatatt aaaatattat ttgctcattg tactcttatt ctctcccaaa 540  
 tattcagcga gttttccaga agctatataa catgtggtaa catcttatca ctctgacgat 600  
 taatagaata tgnnttttg gattcttngn tttaaaattt tctcactttg gggttctaatt 660  
 atggnnacga ttaatagata tggntccat gaccagang ctttaaagca ntcaataatt 720  
 ttttaagagac taagnactat cttttaaaga tngngaactc catcttaatt 769

<210> 652  
 <211> 267  
 <212> DNA



232

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(267)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 652

nnangccctt	taaccattgn	ggcctccacg	cnntggcggc	cgctctacaa	ctagnggatc	60
cgcnaactcta	gnanaangat	tggctcttnt	gggntgggccc	ggncgggctg	gggcgttaag	120
cggggctggg	cgcgcgccgn	ggttgnacna	ggcgccgcgc	ccncacacn	ccgggagcac	180
cctcnttgen	gccntncccc	gctcaccccg	cgcgcgccgn	tccgcttttt	ccncacccan	240
agcncntttt	atctntgtct	cctccgg				267

&lt;210&gt; 653

&lt;211&gt; 501

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(501)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 653

cccnttnacc	cattgtctgga	ctccaccgcg	gtggcgccgc	ctctanaact	agtgggatcc	60
ttncnatgag	atngcgagang	gaggacnnat	ttgctatnct	ggatggggct	gantcntnta	120
gctnctctag	cancagatgg	gttatcgagg	aagatgactc	caangggcta	nantcctatg	180
cncatcctaa	aanncanctg	ctgtnttcag	agtacgcgac	acatcatcnc	tnatgcattg	240
ntgancaaga	cgggcangtg	cttatcctca	gcgangatgc	ccttaaccan	gagctcgaat	300
ggacntatca	ccntanaggt	acanntnccg	caccacacac	cngcttgcn	cctgacgctg	360
gactggatcn	cttaggccac	caatnccccg	tttnccacat	ncctgggacn	ctananatac	420
tccgangggg	gcccggtanc	caattcgccc	taatactgag	ccttgntacg	nacgctnact	480
ngngtccta	ttanaacggt	g				501

&lt;210&gt; 654

&lt;211&gt; 710

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(710)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 654

gcgnctttan	cncatgctgg	gctccacgcg	gtggcgccgc	ctctacacta	gtggatccca	60
acactgagtc	caccacagna	aaactcanca	ccaggcagac	cccacaactg	cagaatccag	120
gctgcaattc	acagactaat	cntctagacc	cacctcagta	ccagatggta	ccacacagct	180
caaggnttta	ggtttgcgtg	gtanactcaa	tctctatctt	tcaccactgc	cagcctgact	240
tcagagatcc	tgnctctgg	acagtccctca	gtggcaggca	actctcagga	gcctcaggnt	300
tttggcacat	cccagnacca	gccagctgcc	acaggccctg	acctntanc	aacactgccc	360
atgtattcca	gacttctanc	ataccacagt	gccatgctga	ttgcatctat	agangctcag	420
gtgcnctca	aanctgtgcc	tgctgcagna	ngccccacgt	ctctggcatg	ccccaatgcc	480
atgngtggn	acanttgact	tctgggcatg	ntggaattcc	ctaccactga	ncctgaccat	540
aggnggganc	ccattttttt	cagggggggg	gcccggcccc	caattccncc	ntatagngag	600
ncgtanttac	gcgcnnctta	ctnggccngt	ngtttaacaa	cgtcnntgan	ctggggaaaa	660
cccctggngg	cnacccaaat	taaacngcnt	tgcanacat	ccccctttcg		710

233

<210> 655  
 <211> 202  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(202)  
 <223> n = A,T,C or G

<400> 655	
ccccttttnc ctttcancnc ccccgttttg gcngccgcgc acacctactn catccaccca	60
cantcgacca cccgagcttt ttcccgatcc cancatcnat gcngattttt tctntgcntg	120
ctgngcctgc acctttgnta ggtcaagcct ggcccatctt cgacaacttc ctcacaccca	180
acgatgaggc atactctgac ga	202

<210> 656  
 <211> 308  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(308)  
 <223> n = A,T,C or G

<400> 656	
gctgntgaaa gaccacaccg aaaaactctn ctttccgact tccacatgat gatcngcatg	60
tggtgggtgag agacttatca tgacgacatc gcttccnacc atcgcanccn ctgcccgaagc	120
ccattcatgg aggcctgggn anttctgtga ntgacntnga cnctanacnc tnccactgtn	180
tgctatccag acttgnttng aatatnttat tggcnaaana canttncgga atgctgtgnt	240
tgnnccattga angatctgat cactatgaga gggtagggac nncctgctng ctggcantnt	300
ntaaccn	308

<210> 657  
 <211> 696  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(696)  
 <223> n = A,T,C or G

<400> 657	
acnntttcca caatnctggn ctccccgcgg tggcgccgcg gtcgaccagc aacctcagct	60
gtgggtcttg ttacagtaat gagttactgt aaggaaagtg tgacatttcg agcaatttga	120
tttgtttaaa aactagagca gtttcagggg ttcccttgta aatctgtctt atgtgtcttc	180
aatgttcttt cttgaggagt agagaaagga attgttagga atgatgcata aacctaggct	240
tattttatct cgtgccacc cataatcaga gcagattctt gggactatga ccctcatgga	300
gacatgacaa ttgtgtgtgt ggtgggtggg agaaaagagc tgggaatttt tagggctctag	360
aggggtccaat caggactatt ttatggagct ctgctcacca actttaagtg agcaccaggg	420
gtngaaagc gaatcttggg ntcaaaaana caatggnaag gggtaagttg gtatnctgaa	480
ctggccactt cggactctta ttttaactggg tattctcant taaggaggcn nggggtggtct	540
tggcttgtna aggaaagcct gtgcaatgga atgactttaa aaccccccat taaaaaaaaa	600
angntataaa tcttgggtct taanaangaa gcctgggttc tnttanccca ttttncctcc	660
gggaaggnaa atnttcttag gnaanggaag ggaagg	696

<210> 658  
<211> 698  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(698)  
<223> n = A,T,C or G

<400> 658  
ctggactccc cgcggtggcg gccgctctag aactagtgga tccgtgttgg ctcaattctc 60  
aaggctgttg ctgtgcggcc tgttcccac acgtgctgct cagctcaggc aagcaccgag 120  
cttgtgttgt ttcatgctca gcgtggaggc ccctcctcca ggtcgctgct ctgtgggggt 180  
ccatacacct caggctccta ggaggagtc atttagaaag ccagggtttt tctcagagtc 240  
ttagtctctt gtgctgtcat ccatttcaca cgacttgggc cctgctcggg gcaacacagc 300  
aagagaaaag acagggaaaa taagagaggg accttgcaca cacacgctct ggaccacaga 360  
gccctgtgcc cagctcctct gtcaatacag gtggaatctc gtgcaggatc gcagggggtct 420  
gtgatgccac caaagagcag gccgggacag ggtaggaga gaaaggagag ggaagtgggg 480  
gtttctccta cgcactctta ttgcagagg gaaaggcggg tttgtattgg gggtgtcgg 540  
ctttgcaccc acngcacagt tgtgagacac ccccatcctn agatcaaagc cccacataca 600  
gcttggggaa aaacaaaacn aaacaaaaca aaaacagtaa acctccatgc canttgttgg 660  
gnaagttttn aatttntctc ccnaccan cttgcttc 698

<210> 659  
<211> 750  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(750)  
<223> n = A,T,C or G

<400> 659  
ncaanctggn ctccaccgcy gtggcgccg ctctagacta gtggatcctc ctcatgggcc 60  
tgatattctc tgaacatatg atgaacattg cttatgaaaa attatttcta ngaaaattgt 120  
gaggcctaag aatgntattt tcttttagtg atggctcttg tttgcttctg taaggnaatt 180  
gtgggcactc gtaagcttgg atctctttaa tctaatacca gntttgagat tttcttggcc 240  
ccatagatga attaaaactg gcgtacttct tgtttacaag anggataagt ctctagggt 300  
aagtcttttg ggtcccaag tcaaaaagat gagggattta ccagtctctt aaccttggta 360  
gccccagact ccaaactttg ccttctagtc ccaagaggct atcaaaaagc aaaggccatc 420  
ttccaccttc ttttccanaa cagcacacat tccagacagt acttgaaagc aggaacctcc 480  
ttatccctta aaaacctctt ggaancatct tccctctctt gcttctacta tgcttggccc 540  
acctancatt cncntttttc tggaaccggy aaaaancttn tgacttngt tggctacatt 600  
cagcttggcc ccctacaatn tggtttccat ctgcctaant gaaattttaa agggcacttt 660  
ttttntggcc cctgactttc nntttttagg gcttccccc angctttgcc cctttggtta 720  
aaggggttat tttccttccc ctttggaaag 750

<210> 660  
<211> 849  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(849)

<223> n = A,T,C or G

<400> 660

tcggatccac	tagtccagt	tggtggaatt	cgcgcccg	gtcgacggg	agtagtggt	60
tgcntntcta	aatgttataa	ttatttcaga	attactctgc	cagaaagtta	tgatcataca	120
tagaagagtt	tgtagctaac	tttgaaagta	gtggaaagt	gttttcagt	attgtttggg	180
ttaatTTaat	tttgattata	tttggttttt	agttcaggta	atttttttgt	tgaaaacttc	240
aaatgacaat	ttcttcattg	ttactaaaga	tcactcatgt	ggagtagttt	cagatttttt	300
tctgaataca	tgtattactt	ttagagatgt	aaagatgtga	aattactaag	agagaaaccc	360
atgtgatttg	tttagtggt	caaaagtcgg	tagctccttt	gacctaagt	gccactgata	420
gttaaataga	tactgaagct	atgggcaggc	tggttgata	agaaaaagg	agacagagaa	480
atgggaaatt	gggaaagaac	tgtgcaaata	ggaaaaggag	agagcaacag	aacagaatta	540
gtaccacagt	gccgaagtgc	cacctcaggt	acttccatct	cccatctcct	gaagaattca	600
gtaacagttt	gcaaatggtc	aacacaatca	tttagtgatc	ctggttgata	ttttcaatac	660
tttctgggga	tttctgggct	ggnttcaaaa	gatgatgctg	atagttttat	tgccctgaa	720
ggtattctga	agnttancat	aatttattgg	tcagtaaaat	atttgaataa	aagngganga	780
aggaaaatct	ggcntcttat	tttgggatnt	cngcnggggg	aangaggata	taattnacc	840
cgcccttg						849

<210> 661

<211> 653

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(653)

<223> n = A,T,C or G

<400> 661

aacttaagct	tggtaccgag	ctcgatccc	tagtccagt	tggtggaatt	cgcgcccg	60
tcgacctcca	ttcgtttctt	gtcctttttt	ttcatttttt	ctcatgttct	attcacttta	120
ggtttctaag	ataaatatta	taaaataatt	tttacttata	aattattcac	tgataccctg	180
tccttaacat	gtgaaatgaa	ttcaaaaagga	atcttaatga	gaaataatat	actcatgatg	240
tttaatatag	ttgatttcga	aataataagc	cctctgaagt	cctaagttaa	aaataaagca	300
actgttttga	taatttttca	tcaagaatgt	atctgagtct	ctgagtaatt	attagtagga	360
atattccatt	atcacaatta	cacagtataa	gctatttagt	ctaactttac	caaaaaagg	420
agctacttca	acactgtgtg	agacttttaa	tggttttgca	ttgggtatgc	actattagca	480
agataaccta	ttttacagca	gtgtttntta	acctttccca	tttatttgaa	aggcagctaa	540
gatatagtag	ttaatntaan	gggctgatgc	atttatatta	catgtagana	atgggagata	600
cnaaaggag	nggggggana	tnttttgnat	tcnnaagctt	cnttgncaat	taa	653

<210> 662

<211> 646

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(646)

<223> n = A,T,C or G

<400> 662

aaacttaagc	ttggtaccgg	agctcggatc	cctagtccag	tggtgtggaa	ttcgcgccg	60
cgtcgacca	gggacaggca	gccagngctg	gggtcaccag	ggtccctct	tgggccctcc	120
aanagcaaca	gtactggcaa	cagctgggat	ttgtgagca	cagactctgc	agcaggctcg	180
gttgagctct	ctgtgcctgt	tccttcatac	catctcacg	ccatccatg	agatgggtcc	240
agctgttttc	agatgagaaa	atggcacagg	aagctggtaa	gtgacagtca	gaaatgaatg	300

236

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ctggcagctt antccttga cccaccgcag tgcaggacct tgctcaacag ggatcaccct 360
tgtccgccac ctgttcatga ggccaccag ggtttgtgtg gtcatttgtc tcctttcatc 420
tgcttgccct caaccagctg ggtcattagg gctggggaac ccagacccca cacagtcctt 480
ctcccagang ccagacacan nctncgccac agnaaggact tcagtccccg aancaaatgt 540
ncctgggctg anaaactgna gggnccccaa tccctggtgg ggtactgctt tgcactggng 600
gaattcaccc ctcattgnaa acctttccct nttnnacccc ctaaac 646

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<210> 663
<211> 650
<212> DNA
<213> Homo sapien

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<220>
<221> misc_feature
<222> (1)...(650)
<223> n = A,T,C or G

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<400> 663
aacttaagct tggtagccga gctcggatcc ctagtccagt gtggtggaat tcgcggccgc 60
gtcgacgtcg acgcggcgng ccgtttcgac gcagttgata catattatta tatactacat 120
nggttttcta gaattaaaaa attaatgtgt agtgccagcc ctagatgtaa gttacatata 180
tcaactctat ccaattttgt cagccataaa acttaccttt ttcacatact tctaactcta 240
acaatgtgag aaatgtagat cattgcaatt ataccacaa ggcagatggc tacatgcaga 300
atggatagca gaatctagct acttacgcta gccacatggt agacgttttt tcctttgttt 360
ttgcaaaatt gcaatataag ttgcataatc ttagagttaa aagatgtaa gaaccatag 420
aagccagtga tgaaggacat ttatatattc acctttacaa angacctaa aattgcctat 480
gtggagcaga aactggagga gggcnaancc atongtaaaa aaaattttgn tncatatttg 540
atttgggcac cattattacc tccccaggtt cctttttgnt ttaacctttc ttttaaaaaa 600
aataattcnt aatttttggg caaaaaaaaa caaggttttt attTaaattt 650

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<210> 664
<211> 678
<212> DNA
<213> Homo sapien

```

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<220>
<221> misc_feature
<222> (1)...(678)
<223> n = A,T,C or G

```

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<400> 664
taaaaaatcta gactacacta ggaaattatt ttantatcag aagaatatca ggggtgtagt 60
actcatcana gctaaatgag agcgctttta aaatgttagt ttgtcttccg ccatttctac 120
agaaagctgc aatttcaggt tttcaacctt ataggtgata ttttaaaaaa aaaaaaagca 180
atcgcaaata gcccactgc ttttacaat cattttttct cttctaggta tagcctgtca 240
ggtggcctaa tgtaattttt gacatctcta ggaattttta tagaaccaga aatgggtgcc 300
agagatatgc ctgcactaat cttaagtggg gatattatgta tttctcaagc aagtgattaa 360
agcaaaaacta ggcacgattg aaatcaanat cttttaggca agaaagtcac gatgagtttt 420
anaattattt taggactctg tggctttctc ttcatagaaa tagaaaaaaa aaattgtata 480
aaaaccacaa aaggtcctga atagcccaaa gcaacactga acaaaaangaa caaagcagga 540
agcaacacac taccggaatt caattatact accaaggtgt antaaccaaa acagcattct 600
attgggcata aaatagacca aagaccagtg ggaaacagaa taaagaancc caaaataaat 660
cctatatatta cngccnc 678

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<210> 665
<211> 694
<212> DNA
<213> Homo sapien

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<220>  
 <221> misc\_feature  
 <222> (1)...(694)  
 <223> n = A,T,C or G

<400> 665  
 cttttcaaat catttttntct cttctaggta tancctgtca ggtggcctaa tgtaattttt 60  
 gacatctcta ngaattttta tagaaccaga aatgggtgcc agagatatgc ctgcactaat 120  
 cttaagtggg gatttatgta tttctcaagc aagtgattaa agcaaaacta ggcacgattg 180  
 aaatcaagat ctttttaggca anaaagtcac gatgagtttt agaattattt taggactctg 240  
 tggctttctc ttcatagaaa tagaaaaaaa aattgtataa aaccacaaaa ggtcctgaat 300  
 agccaaagca aactganca aaaagaacan agcagggaag caacacacta ccngaattca 360  
 aattatacta ccagggtgta gtaacaaaa cagcatttcta ttggcataaa atagacacca 420  
 agaccaatgg ancagaataa agaaccocac aaataaatcc atatatntac cgccanctga 480  
 ttatcaataa cnaacaccaa gaacatatnt taagggaacnt nctattcaat aantagtgt 540  
 ggnaaaaact gggaaatcca tatgcagaaa naatgaaact agacccttat ccctcaccat 600  
 acgcaaannt caacttcgga atgggattac aaaacttaag acattccaac ccaagaaact 660  
 atnaaancta ctattaagaa aacagatcnc nccc 694

<210> 666  
 <211> 705  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(705)  
 <223> n = A,T,C or G

<400> 666  
 tttaaaaatt tagatacact angaaaaatta ttttagtatac agaagaatat caggggggtgt 60  
 agtactcacc agagctaaat gagagcgctt taaaaatgtt agtttgtctt ccgccatttc 120  
 tacagaaaagc tgcaatttca ggttttcaac ctaatagggtg atattttaaga aaaaaaaaaa 180  
 gcaatcgcaa atagcccccac tgctttttaca aatcattttt tctcttctag gtatagcctg 240  
 tcagggtggc taatgtaatt tttgacatct ctaggaattt taatagaacc agaaatgggt 300  
 gccagagata tgccctgcact aatqtaagt ggggatttat gtattttctca agcaagtgtat 360  
 taaagcaaaa ctaggcacga ttgaaatcaa gatcttttag gcaagaaagt catgatgagt 420  
 ttanaatta ttttaggact ctgtgggctt ctcttcatag aaatagaaaa aaaaattgta 480  
 taaaaccaca aaaggtcctg aatagcccaa gcaacactga acaaaaagaa caaagcagga 540  
 agcaacacac taccagaatt caaattatac taccaggtg tagtaaccaa aacagcattc 600  
 tattgggcnt aaaatagacc naagaccaat ggaacagaat aaagaaccca aaataaatcc 660  
 atatttttac agccagctna ttatcaataa aaacnccaag aacnt 705

<210> 667  
 <211> 817  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(817)  
 <223> n = A,T,C or G

<400> 667  
 nnangacttt tgtggtntta tacaattntt ttttctattt ctatgaagag aaagccacag 60  
 agtcctaaaa taattctaaa actcatcatg actttcttgc ctaaaagatc ttgatttcaa 120  
 tcgtgcctag ttttgcttta atcacttgct tgagaaatac ataaatcccc acttaagatt 180

238

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agtcgaggca tatctctggc acccatttct ggttctatta aaattcctag agatgtcaaa 240
aattacatta ggccacctga caggctatac ctagaagaga aaaaatgatt tgtaaaagca 300
gtggggctat ttgcgattgc tttttttttt tcttaaatac cacctattag gttgaaaacc 360
tgaatttga gctttctgta gaaatggcgg aagacaaact aacattttta aagcgcctctc 420
atttagctct gatgagtact acaccctga tattcttctg atactaaaat aattttccta 480
gtgtagtcta aactttttta aaaagacatg taatccgagg agtttgtaac tcaaaacgag 540
tgcatctagg aggtatcgca agccgtttct ggattaaatt cccagctagc ttgcttgctt 600
agcaggggag ggnaanaaag acatctgcag cctagggaag aaaacctttc gcattgttct 660
tacgtgttta cgttatttta tttcctanaa caaggcngaa ttgggactcg aatgggtcag 720
ttggggtggg ggatcccctg gtncataaaa ngtcanaaag anggtacagg cggaacncca 780
agggtcgtcc tgcatttana ctcggaattt tgggtgcc 817

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&lt;210&gt; 668

&lt;211&gt; 826

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(826)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 668

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cggggggnnt tacgtctctc tggacgcttt tattgtacca gggcgatccc agcccaactg 60
taccattcga gtccctactc ctgccttgct ctagggaat aaaaataacgt aaacacgtaa 120
gaacaatgcg aaagcgtttt cttccctagg ctgcagattg tcttcttcac cgcccctgct 180
tagctagcta gctagctggg aatttaatcc agaaacggct tgcgatacct cctagatgca 240
ctcgttttga gttacaaact ccgcggatta catgtctttt taaaaaagtt tagactacac 300
tagggaaaaat tatttttagta tcagaagaat atcagggggg gtagtactca tcagagctna 360
atgagagcgc tttaaaaaatg ttagttttgtc ttccgccatt tctacagaaa gctgcaattt 420
caggttttca ncctaataagg tgatatntaa gaaaaaaaaa acaatcgcan atagccact 480
gctttttaca atcatttttc tcttctaggt atagcctgtc aggtggccta atgtattttt 540
gacatctcta ggaattttta tagaccagaa atgggtgcca gagatatgcc tgcactaatc 600
ttaagtgggg atttatgtat ttctcaanca agtgattaaa gcaaaactag gcacgaatga 660
aatcaagatc tttaggccag aaatcatgaa nanttttana attattttan gaatctgtgg 720
cttctcttct taaaatngaa aaaaaaattg tttaaacca naaggtctga ataccacagc 780
ncctgaacn anagaacaan gccggagcac cccctcccaa atcccc 826

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&lt;210&gt; 669

&lt;211&gt; 547

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(547)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 669

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cattgtgttg gggaaaaaat gatttgtata agcagtgggg ctatttgoga ttgctttttt 60
tttttcttaa atatcaccta ttagggtgaa aacctgaaat tgcagctttc tgtagaaatg 120
gcggaagaca aactaacatt tttaaagcgc tctcatttag cctctgatgag tactacaccc 180
ctnatattct tctgatacta aaataatttt cctagtgtag tctaaacttt tttaaaaaga 240
catgtaatcc gcggagtttag taactcaaaa cgagtgcac tnggaagtat cgcagccgtt 300
nctggatnaa attcccagct tgctngcttg cttagccggg gggcggtnaa aaaaacatct 360
gcagcccngg ggnaaaaacc ttgcgattgt tcttacgtgt ttacgttatt ttatttccct 420
nnagcaaggc nggganttgg ggactcgaaa tggtagagtt gggctgggga tcgcccttgt 480
tacataaaag ngtccagaa gagggacggg tacaggcngg ganctccaaa ggtcagtc 540

```

tgccatt 547

<210> 670  
<211> 232  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(232)  
<223> n = A,T,C or G

<400> 670  
cgaactatatt agactaccta ggaaaattat tttagtatca gaagaatata aggggtgtag 60  
tactcatcag agctaaatga gagcgcttta aaaatgttag ttgtcttcc gccatttcta 120  
cagaaaagctg caatttcagg ttttcaacct aataggatgat atttaanaaa aaaaaaaagc 180  
aatcgcaaat agccccactg cttttacaaa tcattttttc cccaacacaa tg 232

<210> 671  
<211> 214  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(214)  
<223> n = A,T,C or G

<400> 671  
ctccccttcc ntccttcgct actnncatt ttcnnaaatt tntttcgcnt atgnggaaaa 60  
acaccacat tnttcancct gcacagaaca ngnnnggggtg tgtaaaatga agggcttccn 120  
cnctttctct tattnaanaa cactnaaana gggangggct aaaaccgcg ngatntctac 180  
nctatcgcg gcgcttttgg ngttggctag aaga 214

<210> 672  
<211> 328  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(328)  
<223> n = A,T,C or G

<400> 672  
ngancagcgg ngtttaaactg ggcctctaga ctcgaggaga cncctgttgg atggtggatc 60  
acanctcgt actactatac aggacagagt atcggganct cttggntgtt ggngcctgcc 120  
aaccactgct nctgttaact gcgtatctga agggactcgg actggcttca gaagaactac 180  
cggtcgaat gnaccatgga tgattcnnc tagttgaaaa aaaactcagg cacatgtatt 240  
gccactgatg actagcgcca gactnctctc ggctctntaa cgagcccaca tgncngtgtg 300  
ncncccgctg tgnctccaga agaggttc 328

<210> 673  
<211> 223  
<212> DNA  
<213> Homo sapien

<220>



240

<221> misc\_feature  
 <222> (1)...(223)  
 <223> n = A,T,C or G

<400> 673  
 ggggggcaaag ctggctagcg tttaaactta agcttggtac cgagctcgga tcccnagac 60  
 attgtgcatg aaaatgcaaa ttgagtgtgg tctatantgc catcntcacc tnetgncngc 120  
 tcaaaacaac ngctttctgc tgcaatgggt agggctcctn acncacggtc gcnnacggag 180  
 gccncttat cctntcggg nnggatccct ngaagcatnt tot 223

<210> 674  
 <211> 256  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(256)  
 <223> n = A,T,C or G

<400> 674  
 gnggggtcnt ngatgagcgc gcgtaatacn atcactntcn ggcnngntgg gtaccgggcc 60  
 cccctcnaa gcggcgccc ttttttntt tttttcatn acatgataa ntctttnttc 120  
 taaacagacc acaccactan agttcctttn ctttngtacg gaattgagtt aaagtagagn 180  
 atacaatgca gggcttcnnc tctatttcac attccaggnt ggttcngnat ggatcggcc 240  
 tgctctccg atgggt 256

<210> 675  
 <211> 439  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(439)  
 <223> n = A,T,C or G

<400> 675  
 nnactagtc agtggtgtg aattccattg tgttgggctt gtatgggttt tttgtctag 60  
 ttntttggga aatgttngtg ttactatntt ttggatatna tatatgatat gtatggccct 120  
 tctatgggct cctcanacng aactcaacca tttccacaa aaccnattcc tctttccct 180  
 tcatgactga gtggtgttgg tactatccng gaaactggga cattgtcctt cacatctntc 240  
 ccttanctgc ctngtccnat tgatgtcttt gagctntgan atgtctttgt taactntctc 300  
 ctntctctgt actgccggca naattaagca ccatntgtca caaaaagtat tgcgttacct 360  
 tcacgnatct gtngttncc atncttgctg cttctccngn ggaaaatagg ctnttctggc 420  
 aaccgaacng aanaaatac 439

<210> 676  
 <211> 587  
 <212> DNA  
 <213> Homo sapien .

<220>  
 <221> misc\_feature  
 <222> (1)...(587)  
 <223> n = A,T,C or G

<400> 676

```

nggngggcctn attaagcgcg cgtaatacna ctcaactntgg ggcgaattgg gtaccgggnc      60
cccctcaagt tnatntgccn aacctctctt ttggaataac aaaagggtta acacatatgt      120
cctcataggg acgcgctttc acacnttctt gacngcttca tanacntcat tntctatttct      180
cctcagnaca agtttaggcn gaagggtgag canacnttat aatttccatt tcacaaatnc      240
ggaagagtgg gctcaaaggg nttaaaaaat aacctgatac aantcataga gccgggntct      300
ggaanaagca ggagcaaagt ccaggcatcc tgatccaagc tnggtccact gccttccact      360
ctggagaggc ttcattctccg acaaaggaag ggacntgagt ggctgganaa tctcatggga      420
taaagacctc agnatttcat gctcctggaa atccccatgg ttgaacaaca ggtntttggc      480
ccgtgggttct ntccctttgn ccatctttta accttggggg aaatgatggc ntctntnagc      540
nttttttttn aaagagatng aaattgaatg attatngct cattggg      587

```

```

<210> 677
<211> 444
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(444)
<223> n = A,T,C or G

```

```

<400> 677
gtggggcatn attaagcgcg cgtaatacga ctcaactatag gggcgaantg ggtaccgggc      60
ccccctcgaa gggcgccgcc tttttttttt tttttactgt ccaaactntc tatngatnta      120
gttgaaactgt ncaacgattt catgaaattc tatacacana gccttcagggt ccagagagta      180
aaacaaattt aaatttnttc accanattgn agcagncana agcatccnat natatccgac      240
tacaatgaat natatgctna nggtanctna tttaccctact ntgggggtctt tanggtctgt      300
cacaacttat tttcgtaaac atcnntttta anttnggtga atggacctaa tnccagataa      360
ntctatttna tntacccctag catncctgtg gctnactttt cgggctgtgt tggcntactt      420
ttaggagaaa attggtataa atnn      444

```

```

<210> 678
<211> 670
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(670)
<223> n = A,T,C or G

```

```

<400> 678
actagtccag tgtggtggaa ttccattgtg ttgggagcag tttaaaaaaa aaaaagacna      60
aatatacnac tcttgatnaa acataaagggt acagtgggtct atgaggaana gaaaaggtag      120
ctnaggatgc aaaantacct accacatggg aaccgttngt ccacactcat tccnnanaaa      180
accgagtcct ctcanttnca cacgtgtacg tttcagttgg gaagtgcttg ccattactcc      240
naagcctaga accttcacgt cctgaagggt ctggaagggt tttcagattg cttaaganac      300
gcngcccttc catattcttc tccactaccg nggggaacgg aacaaatgga gctgcgacng      360
ggaagcgtcc cttcccntcc gaacgctttc tttcaaacct gcctgccttc cnggcgaatg      420
gaccggaagg tttctnngct tcctttcanc ccnaattact tcctgngttg aaaattggcc      480
tgtttggttg caaatgcngg aatttgttta ctttcntcat gtccctgtgt gnncnaaccg      540
gctcncttgt tgcctccctt tngaaagggt ttcatcaggc cccgcctttt ctcttntaan      600
ngtcctaadc cggncnggac cactcgggga aaattttttc ttttcgaaaa gccgccccnt      660
ccgtccggct      670

```

```

<210> 679
<211> 449
<212> DNA

```

242

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(449)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 679

actagtccag	tgtggtggaa	ttccattgtg	ttgggagtag	gtctactaca	ncctacttcc	60
cctatcatan	aagancttan	caacnttcat	gatccccccc	tctannocct	tttctctanc	120
tgcttcctag	tcctgtttgt	cctnttccta	acantcntaa	ganagatnac	taatnctact	180
atctctnacc	tcgggaanct	acaanacgtc	tggaactatt	cngaccccat	gcancncat	240
nctccatcgt	cctcccagcc	cctncccttc	ctttacntta	ctnaacgaag	gtcgacgatc	300
cctccentac	ctcccnnncc	attgggnccc	aanggnactg	gacctcacga	ntacaccnac	360
tacggggnga	ctaagnctgn	aactccttac	atatntcccc	gttaccctccn	gaacncagcg	420
aacngcnaca	ccttggaant	caagaanta				449

&lt;210&gt; 680

&lt;211&gt; 670

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(670)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 680

tttcngtggtg	gtggaattcg	cggccgcgtc	gacgagaaga	nggaggagga	naaggagaag	60
gagaagaagg	agaanaagga	ggagaaggag	aagaaggaga	agaaatcatc	atcatcatca	120
tcactgtctc	ngcaactatt	taagtttgc	antcccttga	aaacaggtac	ttttgtttca	180
atgtttggga	ccactnctga	cnatgannag	aanaccaata	aatgcttgat	naatgaaaaa	240
nccacttttt	acctgttaga	accctgaggc	taagagaant	gatgtgactc	gacttagtta	300
ccacaaaacta	tgatcctagc	atnaattggg	gcactctcaac	acctcaactc	cctgtgcaag	360
aacagatttt	caatgtctac	tgatgatatt	aaatggatta	nttcctctct	ttacttctta	420
agggcatgaa	gntttatgaa	acaaaactat	ncagttccag	acgcttaacc	cacatagtgt	480
taatagtcat	cttcaacaca	cnactaaacc	cccaaaaaan	gnthtttacg	gngtttcgac	540
agttttcttt	tccttttgac	ttgnttaaca	cccnngacaa	ctttgtntctn	tttccntgaa	600
tcacancctt	onaanancca	atggtnccgt	tttttctont	tengggccct	tccttnttn	660
aaaaccanac						670

&lt;210&gt; 681

&lt;211&gt; 494

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(494)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 681

tcatggtgtc	cacagtctga	tgtgagcgca	ttaaatttaa	ggatctccgc	ccttctcctt	60
aaaactcagg	acttggaat	gancctagga	agcgcccttc	ccctccccc	ccanaccaa	120
gccccggacc	gctgcgnctc	cagctgcgcc	tagtgaaacc	gccgaattcg	aattcacact	180
cggngggccg	gcgaaggtgt	gcgcgcccgc	gggagcgccg	gggcnagccc	gagggactgc	240
aagccaanaa	nggaggcatg	ggtggcgggg	ggcgccgtct	gatccaggaa	ggagcgagg	300
cgccgatcac	acactcttna	gacgcctgc	ccgcgcctgg	ccagcgcgca	gnctgcagg	360

243

```

cgcgcgaggc aggaactcgc tggagtttgc caagccccc gnctctggaa agtntgtagc 420
tccctttcgg ancgncctctt,ctggcccttt gggacgggtg tgtcattggg cgggggtctg 480
tataaggggg ggac 494

```

```

<210> 682
<211> 263
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(263)
<223> n = A,T,C or G

```

```

<400> 682
tgatcattca agcngtgngc gnataacgat tgctnagccc aacctttcat agggtcgttc 60
ctttgggaat nggatgtcta ttgaatggca gggatagggg cactcggcat tcgcctcttg 120
tacagttttg catatatatc ctcatcgga gcgagcgtag gggancgtta agtttgggga 180
aatgccnccg catgnccctn ccggagctta aacccccaac aatnccatt ttnaaaaaag 240
ntttnttant taaaaaaaaa aac 263

```

```

<210> 683
<211> 255
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(255)
<223> n = A,T,C or G

```

```

<400> 683
cttgcccggc atgcacagac ntntttacgg acacnctact ccaagngagc ctgnanctgt 60
ctacgggtcaa nctctaaggt tngncantgc cacanatggc atagtccga gggcggtnan 120
tctggantgc tctctgcaact tgaacntaaa gcgcntttca aganaggncat aatngcctgc 180
ctcttgacaa cnaacaancc cacaccnacc tangaccctn tangcaagga ctggattctg 240
naaatgcaat acaca 255

```

```

<210> 684
<211> 922
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(922)
<223> n = A,T,C or G

```

```

<400> 684
acccttcatt tcatgtgctt ctattttcct acatctttta catgactaag ggattaatga 60
aatcacctct tcataatcat gaccataatt tcatccaaca agtactcaag tttggtgtta 120
gcactttatt aatgottacg aattctctct ctctccctct ttctcttttc cttagtccct 180
gcacaataag gattttttgaa tgtataatat catcttaggt aagctttcat atggtttttg 240
catatgaagc ttatgactgt cataagccat accaagcctg tggagtatgg catgattttc 300
attacataat ccaatgaaaa tagacttatt ttaaatccct aactttgtag ttttaatttg 360
tattttcacta tcttgaaatt aacagctagt acttatccat cacagcagtc tcctactgac 420
atgaagcaag ttgttgaatg cagtaganca tgaatgaaag catttaatgt tanacaaaaa 480
tggggtgatac ccaagcattc tgaattattt gcatcaagga atgggacatg tacattagt 540

```

244

```

gcatcatttc taccaatatg tgacttgaat tggtttttta aaaaaaggan aatgantttc 600
tcaatttgct ttaaaaaaatt ttnaaaaagt tcaatggcat gctgctttgt ctggacttaa 660
tttattaaca attnttaanc cttccttaag gacanaattt tgggtgttcag gatcncctg 720
aagggtctta tttttnatan nattccaaac ccaaaaagggtg gtttaaaatg ggnggggttcc 780
cccnncnaaa atttggaccg gcttttttat atttaaaaaa nttncncttt gngtttgaaa 840
nctnaatacc aattaagggg gaattttacc tnccagtggg aaaaaaaaac nctngcnctt 900
naaaaaattc ccnggagnca at 922

```

&lt;210&gt; 685

&lt;211&gt; 531

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(531)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 685

```

tgaggctctg taaaactgtt cctctgctag gcatacttca tattctctat attaaactca 60
tccttaattg gcatggaaga ttcatgttgc caaatctcag atgaagatcc tatattggat 120
gcaattaagc ctggcagcgc cctcaaaaga cagtcttgct actgctagcc acagccagga 180
cacagtaaca gttccttcta gtgaccnag accataanaa atananatct aaagaattct 240
gactccaaag gcattagccc attcctggta ttgccaatta tgatagaaaa aattgccaaag 300
ctcctgggac atggaaatac actcagtaca tttgagaact ggagaactan tttccaaaat 360
agtatgaaga catganggtg attgtagata tntgagtttg gagaanttga gggaaatcng 420
attacacatg tttactacaa gagatgttna taagtaaaga aggcctgata tacaatctaa 480
cagacnantg agataaatct taantcacia ctgaentccc ttttggggcg g 531

```

&lt;210&gt; 686

&lt;211&gt; 336

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(336)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 686

```

ggngncctna tgagcgcgcg taatacgatc atatagggcg aattgggtac cgggcccccc 60
tcaagaacac tacaagctat gtcctcttct canagagccc tgaantttta acatattgaa 120
agctctnate ttgccaaana actccactta acttcaaaac acaccctcca cacacatcat 180
gatcaactna gatcttactg aaccagaatc ctnaatggca tacttcagga acaggggtcc 240
anagaagcag ttctcaaanat gcagctnaaa aagaaactga aaaccaatt catgcaanac 300
ctagggctta tttgagagca ttttccagtg cagatt 336

```

&lt;210&gt; 687

&lt;211&gt; 271

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(271)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 687

245

```

aatctgcact ggaaaatgct ctaaaaataag ccctaggtct tgcattgaatt gggttttcag      60
tttcttttta agctgcactt tgagaactgc ttctctggac ccctgttcct gaagtatgcc      120
atattaggatt ctgggtcagt aagatctcag ttaatcatga tgtgtgtgga ggggtgtgtt      180
tgaagttnag tggagttctt tggcaagatc agagctttca atatgttnaa acttcagggc      240
tctctgagaa gaggacatag cttgtagtgt t                                     271

```

```

<210> 688
<211> 740
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(740)
<223> n = A,T,C or G

```

```

<400> 688
tgatgaagcg gcgctnntac nactcactat nggggcgaan tatgggtacc gggnccccct      60
cgaagcggcc gccctttttt tntttttttg tgagagttta aataaaatat ttgagtttaa      120
tttaaagttt gagtttaatt aaaatatatg gcataatcca agttgggctt tgcanaaaga      180
acactttctca ggaaactgta gttggtgtac caggaactca gaagggtcct gttattaaat      240
atatttgtaa aatgcattga ttctctgaan atcncctctgc atgtgagcaa cacttacatc      300
ncaaaccaaa attggcattg catacatnaa ccaatatattc ccaaacattt ctgggttatgg      360
cccaccccct ttgtgtanta cttattgctg ttttttgtaa ccctggggaa attacttaaa      420
atattcagct ggaaattaca ggcgttactt ttaagggaanc aagaattaca gtgactccca      480
aaattgcaag tgttgattac tatttaagaa cccaagaatt tgaaagaaat ttgaaaagt      540
gaaaaacngga aatnttaaat gacttctcaa attttgaaaa ctonggnaaa catctccact      600
ttggtncctt tcctttaaaa attggctaaa aattntttnt tatncccacc ccattggaan      660
tncccccccc ctggaacaat tggattcccc tatttcctaa aaaacggccn ccccccccg      720
gngaacncc nacnttttgn                                     740

```

```

<210> 689
<211> 635
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(635)
<223> n = A,T,C or G

```

```

<400> 689
actagtccag tgtggtggaa ttccattgtg ttgggattac atatactttt agcaattttt      60
aaagaagtgt acaaagtga gatgtttcct gagctctcat atatctgana atgtcatttt      120
acatctccgt cttcacctct caaaacttct ttcaattctt tggctcttaa tagtaatcaa      180
cacttgcaact ctggagtcac tgtaattctt gctcctttac agctacncc tttatttoca      240
gctgaatatt tttagttatt tcccagggtt ccaaaaaaca gcaataagta ctacacaaag      300
ggggtgggcc ataaccagaa atgtttggga aatactggct catgtatgca atgccaaatc      360
tggtttgcna ttgtantgtt gctcacatgc agagtgaatc ttcaaanaat ccatgcattt      420
tccaaatata tttaataaca gggaaacctc tganttcctg gntacaccaa ctaacagttc      480
ctgaaaaatg ttctttctgc aaaacccaac ttggggatat gccatatatt ttaattaaac      540
tcaaacttta aattaaactn caattatttt attttaaaact cctcaaaaaa aaaaaaaaaa      600
agggggggcc cttccaangg ggggnccggt tcccc                                     635

```

```

<210> 690
<211> 3923
<212> DNA
<213> Homo sapien

```

&lt;400&gt; 690

acagaagaaa	tagcaagtgc	cgagaagctg	gcatacagaaa	aacagagggg	agatttgtgt	60
ggctgcagcc	gagggagacc	aggaagatct	gcattgtggg	aaggacctga	tgatacagag	120
gaattacaac	acataacttt	agtgtttcaa	tgaacaccaa	gataaataag	tgaagagcta	180
gtccgctgtg	agtctcctca	gtgacacagg	gctggatcac	catcgacggc	actttctgag	240
tactcagtgc	agcaaagaaa	gactacagac	atctcaatgg	caggggtgag	aaataagaaa	300
ggctgctgac	tttaccatct	gaggccacac	atctgctgaa	atggagataa	ttaacatcac	360
tagaaacagc	aagatgacaa	tataatgtct	aagtagtgac	atgtttttgc	acatttccag	420
cccctttaaa	tatccacaca	cacaggaagc	acaaaaggaa	gcacagagat	ccctgggaga	480
aatgcccgcc	cgccatcttg	ggtcatcgat	gagcctcgcc	ctgtgcctgg	tcccgcttgt	540
gagggagagg	cattagaaaa	tgaattgatg	tggttcctta	aggatgggca	ggaaaacaga	600
tcctgttgtg	gataatttatt	tgaacgggat	tacagatttg	aaatgaagtc	acaaagttag	660
cattaccaat	gagaggaaaa	cagacgagaa	aatcttgatg	gcttcacaag	acatgcaaca	720
aacaaaatgg	aatactgtga	tgacatgagg	cagccaagct	ggggaggaga	taaccacggg	780
gcagaggggc	aggattctgg	ccctgctgcc	taaactgtgc	gttcataacc	aatcatcttc	840
atattttctaa	ccctcaaaac	aaagctgttg	taatatctga	tctctacggg	tccttctggg	900
cccaacattc	tccatatatc	cagccacact	catttttaat	atttagttcc	cagatctgta	960
ctgtgacctt	tctacactgt	agaataacat	tactcatctt	gttcaagac	ccttcgtgtt	1020
gctgcctaatt	atgtagctga	ctgtttttcc	taaggagtgt	tctggcccag	gggatctgtg	1080
aacaggctgg	gaagcatctc	aagatctttc	cagggttata	cttactagca	cacagcatga	1140
tcattacgga	gtgaattatc	taatcaacat	catcctcagt	gtccttgccc	atactgaaat	1200
tcattttccca	cttttgtgcc	cattctcaag	acctcaaaat	gtcattccat	taatatcaca	1260
ggattaactt	ttttttttta	cctggaagaa	ttcaatgtta	catgcagcta	tgggaattta	1320
attacatatt	ttgttttcca	gtgcaaagat	gactaaagtc	tttatccctc	ccctttgttt	1380
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247

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<210> 691  
 <211> 882  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(882)  
 <223> n = A,T,C or G

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aaaataaaac tagtataagg atagaagccc aggggttgatt taagtctgcg gaaatcataa 180
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atctgggatt atttdgatat tttaaaggaa aacgatgact tttagctctc aggatgttag 420
tttccctaac cataaaatga agagcctcga aaagatttctg tttaccagat tatttctgaa 480
gtcaattcca gttctaaaat tccatcactg ngcactaagg caaattgaat tgaataaagt 540
attgggnatg cataaaatc tctattttta aaaangaata gtaattatcc attggnaaca 600
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atcccttaac aaaccgattt tgcaaaggag cttanccttg gggacttgg tcanggcaac 720
tggtctactt tnaagactca tcttcaacta ctgggcacca aatncctacc attgcatcaa 780
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ttttgngggg tttccnaaaa gaatcntccc ccccgagggg cc 882

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<210> 692  
 <211> 235  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(235)  
 <223> n = A,T,C or G

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cttctcanag cacttaatat gttaataata aactncgnga aaaaagatnt tcnatgaanc 180
nttctcttta ggaggtcagg ngagaatagt gttaatgnca ttaagganag aacga 235

```

<210> 693  
 <211> 383  
 <212> DNA  
 <213> Homo sapien



248

```

<220>
<221> misc_feature
<222> (1)...(383)
<223> n = A,T,C or G

<400> 693
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taatgcaccg catctacatt cccatgctct ctttacttct tcagcattgc ctaaaggcat      180
aatacacctt taattaatta attcagcctc ctaatgcaca ttaacaaagc ccctgctaga      240
ctctgtccat aatggnaaac ctgnatgac cttgatatta acantttaag gaatgctcat      300
ggattgggtt cagacttaaa aaattgaggg ggctgaanaa aatctaangg anaaatcatg      360
gaagcatttg cacatattac ata                                     383

<210> 694
<211> 204
<212> DNA
<213> Homo sapien

<400> 694
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actgtccctt atttttttcc ctcccaggct cataactcga ggttaaaactc tcttttatac      120
aagaaccctg tctgatgaag catcatttca gaattttaag tcaacttaca aatgtggtat      180
tattcacatc tgagtacaaa tttta                                     204

<210> 695
<211> 670
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(670)
<223> n = A,T,C or G

<400> 695
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gagacggagg cagaanacag gccccccaa agaaganacc ggaggcanaa aacagggccca      480
ccanaggag gagacggagg canaaacagg gccaccccaa aggaggagac ggaggcaaaa      540
cagggccacc caaaaggagg aagccggaag gaaaaaacag ggcccccca aaggaggaag      600
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ggggcccnnc                                     670

<210> 696
<211> 317
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(317)

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<223> n = A,T,C or G

<400> 696

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gcccactgtc	atcgtaggata	catttcactt	ttttcacatg	actaaggagc	tctccggagt	180
gaagagttag	taaataatgtt	tattacgcat	tcatttgcta	agaatcatca	agaacccaaa	240
gtagagacg	tttcgtggtt	gaactttctc	cctactgtct	agtagaatta	tatggggatt	300
ctggatctgc	tggtgcc					317

<210> 697

<211> 246

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(246)

<223> n = A,T,C or G

<400> 697

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tttttttct	tnacagagnt	ntttttgtgc	ccttggttct	tatgctcana	ctcngcaaaa	180
aanatcaaaa	gntacnnatg	aaaaacntat	nccatctnca	naaaggaggt	gnagntatta	240
ctttct						246

<210> 698

<211> 3674

<212> DNA

<213> Homo sapien

<400> 698

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&lt;210&gt; 699

&lt;211&gt; 2051

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(2051)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 699

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aaaaaaaaaa	a					2051

&lt;210&gt; 700

&lt;211&gt; 2841

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(2841)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 700

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&lt;400&gt; 702

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&lt;211&gt; 2904

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 703

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&lt;211&gt; 4034

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 704

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&lt;210&gt; 705

&lt;211&gt; 6976

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 705

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&lt;210&gt; 706

&lt;211&gt; 123

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 706

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      20              25              30
Tyr Leu Ala Ser Val Ala Ala Phe Pro Val Ala Ala Gly Ala Thr Cys
      35              40              45
Leu Ser His Ser Val Ala Val Val Thr Ala Ser Ala Ala Leu Thr Gly
      50              55              60
Phe Thr Phe Ser Ala Leu Gln Ile Leu Pro Tyr Thr Leu Ala Ser Leu
      65              70              75              80
Tyr His Arg Glu Lys Gln Val Leu Ile Gly Gln Trp Val Glu Ser Gly
      85              90              95
Trp Glu Gly Trp Ser Gly Phe Leu Gly Gly Gln Leu Ala Gln Asn Leu
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260

Val Ser Gly Lys Gln Leu Trp Arg Met Leu Leu  
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&lt;210&gt; 707

&lt;211&gt; 150

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 707

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 Ala Ala Gly Ile Thr Tyr Val Pro Pro Leu Leu Leu Glu Val Gly Val  
 35 40 45  
 Glu Glu Lys Phe Met Thr Met Val Leu Gly Glu Ser Leu His Pro Pro  
 50 55 60  
 Ser Phe Leu Phe Gln Ile His Ala Thr Trp His Val Gly Gln Glu Tyr  
 65 70 75 80  
 Leu Cys Pro Gly Ser Cys Leu Glu Gly Glu Val Val Cys Trp Glu Gly  
 85 90 95  
 Ile Ala Gly Gln Glu Gly Asp Pro Gly Leu Arg Gly His Thr Lys Arg  
 100 105 110  
 Lys Lys Arg Ile Pro Arg Thr Tyr Pro Ser His Leu Trp Ile Pro Gly  
 115 120 125  
 Pro Ala Gln Ser Leu Ala His Arg Arg His Trp Arg Asn Ala Pro Asn  
 130 135 140  
 Leu Trp Leu Ala Leu Leu  
 145 150

&lt;210&gt; 708

&lt;211&gt; 371

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 708

Met Leu Phe Pro Ser Phe Ser Arg Ser Leu Val Pro Leu Pro Leu Ala  
 5 10 15  
 Leu Tyr Leu Ser Gln Pro Leu Thr His Thr Thr Ser Leu Leu Ala Gly  
 20 25 30  
 Ile Gly Pro Val Leu Gly Leu Val Cys Val Pro Leu Leu Gly Ser Ala  
 35 40 45  
 Ser Asp His Trp Arg Gly Arg Tyr Gly Arg Arg Arg Pro Phe Ile Trp  
 50 55 60  
 Ala Leu Ser Leu Gly Ile Leu Leu Ser Leu Phe Leu Ile Pro Arg Ala  
 65 70 75 80  
 Gly Trp Leu Ala Gly Leu Leu Cys Pro Asp Pro Arg Pro Leu Glu Leu  
 85 90 95  
 Ala Leu Leu Ile Leu Gly Val Gly Leu Leu Asp Phe Cys Gly Gln Val  
 100 105 110  
 Cys Phe Thr Pro Leu Glu Ala Leu Leu Ser Asp Leu Phe Arg Asp Pro  
 115 120 125  
 Asp His Cys Arg Gln Ala Tyr Ser Val Tyr Ala Phe Met Ile Ser Leu  
 130 135 140  
 Gly Gly Cys Leu Gly Tyr Leu Leu Pro Ala Ile Asp Trp Asp Thr Ser  
 145 150 155 160  
 Ala Leu Ala Pro Tyr Leu Gly Thr Gln Glu Glu Cys Leu Phe Gly Leu  
 165 170 175

261

Leu Thr Leu Ile Phe Leu Thr Cys Val Ala Ala Thr Leu Leu Val Ala  
 180 185 190  
 Glu Glu Ala Ala Leu Gly Pro Thr Glu Pro Ala Glu Gly Leu Ser Ala  
 195 200 205  
 Pro Ser Leu Ser Pro His Cys Cys Pro Cys Arg Ala Arg Leu Ala Phe  
 210 215 220  
 Arg Asn Leu Gly Ala Leu Leu Pro Arg Leu His Gln Leu Cys Cys Arg  
 225 230 235 240  
 Met Pro Arg Thr Leu Arg Arg Leu Phe Val Ala Glu Leu Cys Ser Trp  
 245 250 255  
 Met Ala Leu Met Thr Phe Thr Leu Phe Tyr Thr Asp Phe Val Gly Glu  
 260 265 270  
 Gly Leu Tyr Gln Gly Val Pro Arg Ala Glu Pro Gly Thr Glu Ala Arg  
 275 280 285  
 Arg His Tyr Asp Glu Gly Lys Ala Leu Ala Ala Ser Arg Gly Trp Cys  
 290 295 300  
 Gly Ser Arg Pro Pro Glu Thr Thr Leu Gly Ala Val Ser Gly Leu Val  
 305 310 315 320  
 Pro Leu His Pro Gly Pro Asp Phe Ser Val Arg Lys Val Gly Met Asp  
 325 330 335  
 Pro Ile Cys Ile His Gly Phe Ser Trp Val Trp Asn Ile Ser Ala Cys  
 340 345 350  
 Gly Phe Arg Lys Ala Ser Gly Cys Ser Arg Ser Leu Ile Arg Val Val  
 355 360 365  
 Ala Pro Val  
 370

<210> 709  
 <211> 141  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(141)  
 <223> n=A,T,C or G

<400> 709  
 tacggcgtgg tgcggagggc ggtacccac aaataaacn nacaccccat cctatctgtg 60  
 tccacanata aantgactca ttcctctcct cgcatanccc actntcccct ngcgataccg 120  
 taacnaance cttccccctt t 141

<210> 710  
 <211> 196  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(196)  
 <223> n=A,T,C or G

<400> 710  
 cnatccttcn cntacaccca tgangtccat gtgcacgtc cacctcccct caaaacttgg 60  
 gtcncatcc acccgctact ctcccenaa ncnataaccc cttttngcga atagacccca 120  
 ccttancaat nggtttttt tttttgtgcc ctnggnccgn gcgattcaan aaattgaagg 180  
 cccanaaaaa cccct 196

262

<210> 711  
<211> 177  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(177)  
<223> n=A,T,C or G

<400> 711  
ntacntcnct ccnaatgaaa ttcgaanctc ggttaccggg gggnattccg attaggngcg 60  
tantctcgga tgtgcagtc caagtctttt gctaattctt ataattntcn ctacccttcc 120  
ttcnacaata ctgctatcct anttnttctn tcnctctctt cccannttac taaccac 177

<210> 712  
<211> 185  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(185)  
<223> n=A,T,C or G

<400> 712  
aaacgnacca nngccaacga tangtgttg nggtggttgc ggttggtcct cttatntgca 60  
ctggttggtcc gtgtcgacag ganggccacg tccctctgnc ntgagtanca catagcatcc 120  
acgttttagtc gactntnccg ggcggccgct ctaccctnt atngattctt attaaaantc 180  
ggatc 185

<210> 713  
<211> 172  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(172)  
<223> n=A,T,C or G

<400> 713  
nntgggtgcc tgnrcgtnta ctctaaagga tntactatnc atatggantc naanacgact 60  
cactacacgg cnetctnccg agccnnggtc agtgcctnct nggagacctt ctctggggca 120  
ggangagcac tnggtatgtt cacgtatcnc ttcntaaana tacnccctc cg 172

<210> 714  
<211> 112  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(714)  
<223> n=A,T,C or G

<400> 714  
nttgcgtgcc tggacgtnta ctctgcanga tctactactc atngaatc taantacgga 60

263

ctcactatnc ggcancgcag gcgcagcagg gaangggta cctcccagtc tc 112

<210> 715  
 <211> 326  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(326)  
 <223> n=A,T,C or G

<400> 715  
 tactctanag gatctncgng tcatntggat tctatntcga ctcactctag ggctcnagcn 60  
 gtcngccggg caagttattc ggatcgtcgg gntccgagct tcgcaattaa ntgtgccatc 120  
 gttctncaac gttcctgact nggaancccc ngcngttcng atccnccggg acctagctcc 180  
 anntccccgg tntcctttct ggngtntcat naangaggac cncctcgcg cnccttccct 240  
 taatctgcnc acnctgaacg nccaatggac atngtgcgtt taatntanna ggcccgnctc 300  
 gngtgccctt cccgtnannt cagctc 326

<210> 716  
 <211> 122  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(122)  
 <223> n=A,T,C or G

<400> 716  
 nntgcgtcgc ctgngcgtnt actctagatg atctgantag tcatatggat tctaatacga 60  
 ctcannatag ggctctagcg nggatncnga ttcgtctcgc ngattcantg acnccggtan 120  
 ca 122

<210> 717  
 <211> 203  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(203)  
 <223> n=A,T,C or G

<400> 717  
 cntgcatgcc tgcaggtcga ctctagagga tctactagtc atatggatcg agcggccgcc 60  
 cgggcagggtg tnaatgataa anatgcatca tactanccta cagaanggag agataatgtt 120  
 ngntggacca ngttggtttt cttgcgtgtg tgtggcagta gtaagttatt agtttttana 180  
 atcantaccg cctccgcac cac 203

<210> 718  
 <211> 168  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature



264

<222> (1)...(168)  
 <223> n=A,T,C or G

<400> 718  
 ggcagganga tcncttgagc ccngagggtc gaggtacag tgagccanga gtgcactact 60  
 gtncgcccct ccgcatncac gngtggtccg atccccgggt accganctng anttcactgg 120  
 anttcttttt aancgtnttg antggtacna ccctcgantc cctggctg 168

<210> 719  
 <211> 210  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(210)  
 <223> n=A,T,C or G

<400> 719  
 cancgctcgc ataacacgta ttttntgatn aagattctna ctgacccatn aantctacnt 60  
 ctcaagctct tncanngtcc agtnaangga atgtgtatnn gtngggatnc cacanaaaaa 120  
 aganatntcg gncgcttcat tantcatcct tcttaccan ntctctngat nncagntng 180  
 ancntgaacg cacactacng gatntctcca 210

<210> 720  
 <211> 131  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(131)  
 <223> n=A,T,C or G

<400> 720  
 tccatcctaa tacgactcac tatagggctg ccaacctgcc atccactact gaggaagacc 60  
 cgnaactta ggggctcact gcgagccacc ggccacaggt cgtatagggc aaagcacng 120  
 gaagcaccct t 131

<210> 721  
 <211> 121  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(121)  
 <223> n=A,T,C or G

<400> 721  
 tccatcctaa tacgactcac tatagggccg ntgantnctg gcgaaaggct tacaattaag 60  
 naggaaaaan ganccaacaa ctaaaaaaaa nncggncgtg hcagcttnga tgactngtcc 120  
 a 121

<210> 722  
 <211> 246  
 <212> DNA  
 <213> Homo sapiens

265

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(246)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 722

```
anctggagtc ggcgctgca gtcacattgt ggatccanaa aatcggcaca agctctcntg 60
gnttcntcga tatgaanaac actaatccca tgtngtntgn gtctccgtga ttcacccctc 120
gcacnggtcc ccntccnaac cnttgcatag gtgttatgtt gtantctccc cagtgcacaa 180
agattnacac tctctcantg tctganatat gcacgagttc attgtcctgt cnccgtnaac 240
atcaag                                           246
```

&lt;210&gt; 723

&lt;211&gt; 160

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(160)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 723

```
cctccggaaa atccaantag agtaantncc ctctaattccg gggnaattgg nggggttnnat 60
acgtcctcct cccccagnt aggattnana aaaggntccc cagancaaaa nctccaaagt 120
gnatcnanta gccgtncctg anatincaacg cccctacgtc 160
```

&lt;210&gt; 724

&lt;211&gt; 156

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(156)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 724

```
tnanccnata tacaccaaatt tctgattcta aantcccacc caagggaataa agttgagaa 60
gagcctttcc acttttctac taataaaaaa atgcaccagc ccctaccann agtngggaaa 120
acctccttag gcccttgntt ggaacaancg aaaatc 156
```

&lt;210&gt; 725

&lt;211&gt; 347

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(347)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 725

```
aganggttnt atncatgctg tactcgcgcg cctgcagtcg aactagtgag atccaaagaa 60
ttcggcacga gagacggtgc gcgatggacc gagggcccca gccggngagg cgccgcccgc 120
gagcccgcgg ncagacgcc catcagtagc gtccgcaccg ggnagccgcg gntctcgccc 180
gagccgtggg cgcgcccagag gggcgggctc gcctcccgcg gtcctctcga gctctgcggg 240
```

266

gcccagagccc gcgcccgtcgc cgccgcgcgc ttgccgctcg gncgcgcgcg nccggnaaac 300  
gcggtcgagg tctggatgng gcanngcccg cncctntcgc tgagcct 347

<210> 726  
<211> 162  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(162)  
<223> n=A,T,C or G

<400> 726  
ttgggtgggt tgggtggggg naaatttncc catttgggtg ggtttggggg ggnaaatact 60  
tcccgccttt tnggtnccca aaganacnaa gggggagtc cttnatagag gnagngcgat 120  
nctncnaac nacntngact ttgnccatgg ggagnaaggt gg 162

<210> 727  
<211> 120  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(120)  
<223> n=A,T,C or G

<400> 727  
gtgtgggtgg ggaattccat tgtggttggg ggnaaatctc cgcttgtcca aagnacaggg 60  
ggggtcnctt anagnnagg ggggttcctc ccaccacttg ncttgnccat tgnaganaag 120

<210> 728  
<211> 130  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(130)  
<223> n=A,T,C or G

<400> 728  
gaccactgc agcgttnaac ttagcttga ccgagctcgg atccctagtc cgtgtggtgg 60  
aattccatgt gtcgagagag gggcaaatac nctccaanac ancncctca tgctcnacac 120  
atattcgcat 130

<210> 729  
<211> 182  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(182)  
<223> n=A,T,C or G

<400> 729

267

```

cngactgctn gcgtttaaac ttaagcnagg taccgaacgg ggatnnacga ctantgatcg 60
gctggctgct tccagtcgat tanatttgtg aaaaagctga accncngccn gttaaggggg 120
annatgcaaa anatncatcc nnctgccccn taaactgntc tntccnaggg aaaaaangga 180
ag                                                    182

```

```

<210> 730
<211> 678
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(678)
<223> n=A,T,C or G

```

```

<400> 730
cactcncact cgggacctag gcncttcacc actgctctct tctcctcct cctcctcntc 60
ctcggggctg ggggaccttc cccagtgacc atctcacttt ggotgaanoc cactcggggc 120
agcctgagtt tggggctctt ggccttctca ccctcctcgg cccctcctt ggcccgcacc 180
aggccaaacc ggggcagccg taccttgagc ttgtgtccgg cctctccctc cccctctgcc 240
acctggtact cggcatgggt gcccccgga tggcgagagc tccacgtcgg gcagtgaaga 300
gcagaaagta cgctcggccc ctgggggctg ctctcagca ccctcggccc ccaccctagc 360
tctggcccc agtgtgggca acttcagcct cagcccaccc tcgcctgtgg ccgcctcgcc 420
cgctgtgcc tctcggtta gccccacgtc caactcaagc tggggcactg tcacgggtgg 480
catcttaaag acaccctcac ccaccagcag ctaccacct gcaacctggg ctccaggcaa 540
aaaaagggtc acctggggca nctgaacct gtacctgctg tgccctctgc tgaanggaat 600
gttatctgaa cctgctgcc tgggggtact gccttcccaa aaccgggtca antccacctg 660
ttggaaggna aatncccc                                                    678

```

```

<210> 731
<211> 135
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(135)
<223> n=A,T,C or G

```

```

<400> 731
gagatccgac gtcaccccct tccggcggcc caagacgctg caactccga ggcngcccaa 60
atatcttttg aagagcgctc ccagcccaac acaatggaat tccaccacac tggnttagtg 120
gatccgagct aagcc                                                    135

```

```

<210> 732
<211> 660
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(660)
<223> n=A,T,C or G

```

```

<400> 732
gcttggtacc gagctnggat ccctagtaac ggccgccagt gtgctggaat tcggctttct 60
tcaatcagnt nacgagctgc atggtctgct aacattgtca taattgctgg catagattac 120
tgaaaataaa gaaaaaaaaa tgaagctgcc tatcaagttt tggattatc aaaaacttcc 180

```

268

```

tacaagttaa tttacttcaa ccatgttatt acaaatatit taatgaatac tttagagact 240
ttaattacaa aaaactgaga tagtaaaagc aagtaataaa agctgaaatt acttagctat 300
ttgataatta cataaattat tatgttccat tcaacttttc tagtgtttag tttatacacc 360
aggaagactt tcctattcta ctaacattta taaagtatgc taacctatta tttaaacgca 420
tccactatta ggattttatg gcctaaaacg tgatacagtt cagtatcttg atgtcaaaac 480
tttttaagca agtagggatt aagttcaagt gaatgtgatt ttctttcttc ccagtagggg 540
ctttctgaata actcagnaaa gctcacttcc attatcttac tttataaaaa aatgctataa 600
gacagaatgg gccgacgtgg nggctccacc tgtatccacc tttggaggcg agnggcgaat 660

```

```

<210> 733
<211> 836
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(836)
<223> n=A,T,C or G

```

```

<400> 733
aattaatgac tttttttccg ccctgccaag ctagtttgtc taaatataat gtaaagaaat 60
tagctactca ttttctgggc cacgaagggt cctaaaatgg gaagaagtgg agatctgacc 120
ttgttagttc taaatacact aaactgggag tgccatggat ggctttcagg atgtcctgaa 180
tcctctataa ttgtatacaa aatcgtgagt ttttaaaaac tgggttagag ctattgggtc 240
ctcagagtct caggcatctt agaccccaa aaaggtttaag gactactgac ttaaccaatt 300
aggtttgagt ggcattggct ttgaagaaaa gcagaggaaa gatataatit ataattctgg 360
gcaacaaaaa agtggatgtg tgccagcatc ttagagtaga atcctcttaa aaggatagca 420
ctgcatatga actagtaggt ttaaccagt gcatatttag gcgaagtagc tcatttttct 480
gttagaattc ttttttattt gggaatgggc aagcttttac agcttttacc ttgccaatga 540
atacctggaa ttttaaaaaat cttgttaggc atattgocca taaagttttt tttcctagat 600
cataatattc gtaaatatgt ttgtagcttt atttcaatcc cccaattcat tgagggttga 660
aacaatttga atggtttgag tgtagaagct aagttatttc tgtagaggct aagggcattt 720
ataccaanat atgttagact tgnngntcct gttaaccatg ctgtanacaa taggaattac 780
tgtatatcca cattttaatt ttaacatctt ctgctttgnt gntggttga gangga 836

```

```

<210> 734
<211> 694
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(694)
<223> n=A,T,C or G

```

```

<400> 734
nagtnctatt tncactaaac tgnagtgcc ttggatggct ttcaggatgt cctgaatcct 60
ctataattgt atacaaaatc gtgagttttt aaaaactggg ttagagctat tggttcctca 120
gagtctcagg catcttagac ccccaaaaag gttaaggact actgacttaa ccaattaggt 180
ttgagtggca ttggctttga agaaaagcag aggaaagata tattttataa ttctgggcaa 240
caaaaaagtg gatgtgtgcc agcatcttag agtagaatcc tcttaaaaag atagcactgc 300
atatgaacta gtaggtttta accagtgcac atttaggcga agtagctcat ttttctgtta 360
gaattctttt ttatttggga atgggcaagc ttttacagct tttaccttgc caatgaatac 420
ctggaattta aaaaatcttg ttaggcatac tgcccataaa gttttttttc ctatgcata 480
tattcagtaa atatgtttgt agctttatit caatccccca attcattgag ggttgaaaca 540
atttgaatgg tttgagtgtg gaagctaagt tatttctgta gaggctaagg gcatttatac 600
caagatatgt tagacttgtg gttcctgtta accattgctg tagacaatag gaattactgt 660
atatccacat ttttaattttt aacatcattc tgtc 694

```

269

<210> 735  
<211> 126  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(126)  
<223> n=A,T,C or G

<400> 735  
ncnttgaaac nggttgacca gatttcaggc ctgtgcgctc aatcgtggag aatctcgtgc 60  
cgaattcggc acgagtctct ctctctctct ctctctctct ctctctctct ntctctctct 120  
ctctct 126

<210> 736  
<211> 165  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(165)  
<223> n=A,T,C or G

<400> 736  
cagaagcctt taaaccggtt ngaccagact tcaggcctgt gcgctcaatc gtggagaatc 60  
tcgtgccgaa ttccgcacga gtctctctct ctctctctct ctctctctct ctctctctct 120  
ctctctctct ctctctctct ctctctctct ctctctctct ctctc 165

<210> 737  
<211> 125  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(125)  
<223> n=A,T,C or G

<400> 737  
ggnagcccct ttaaccggtt gtccagactt caggcctgtg cgctcaatcg tggagaatct 60  
cgtgccgaat tcggcacgag tctctctctc tctctctctc tctctctctc tctctntctc 120  
tctct 125

<210> 738  
<211> 137  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(137)  
<223> n=A,T,C or G

<400> 738

270

```

ggagncnctt gancaggatg accgacttca ggccctgtgcg ctcaatcgtg gagaatctcg 60
tgccgaattc ggcacgagtc tctctctctc tctctctctc tctctctctc tctctctctc 120
tctctctctc tctctctc

```

137

```

<210> 739
<211> 970
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(970)
<223> n=A,T,C or G

```

```

<400> 739
aggcctattt aggtgacact atagaacaag tttgtacaaa aaagcagggt ggtaccggtc 60
cggaattcgc ggccgcgtcg acggcccttn gtgccactag ntctttcatt cttccccccc 120
atcaatcagt gaacttttta gcctactcaa agctttgtct caatgcatag gatttatgat 180
tgtggggatt tccagataat ataaatattc aacatgaata ttttaaatta aggcattgaga 240
catttttcct aactgagcat agccatgaac ctctcacgtc tgttcctctg tgtcagtttg 300
tancactgaa tacagcagcc ctctaaaag tccaggcagt gcacaggtct tgacatgatg 360
aagtgcgtg ttgctatggt gattttgcag ctggccaaat agtcactggt tgattttacc 420
cagcaggaga tttttgcaaa aatttcctgg gtgagagtga aatcaaaact ctattttgnt 480
tctctctctc aagctgnagt taagatggat taatgagtac ttttagatta attaaactct 540
aagagaaaaa gggagaaaag tgaggaaggt tgttggcaga agtcattgct ggaatccttc 600
tgaaggaggt actgacttca cttgcaaaga cnagagacta naagacaatg aagttaaact 660
tggcctgtct ctcatatgat agatgctgag agtcaggntc agggaaattt aattctgtca 720
tacgcatatn ggattatgtg gtcattggatt tgttggcact aaccngcctn taatcagnat 780
aagaaaagtg ttttggtaga naaagaaaat tatggcccag aaaaacctgg aanacttggg 840
aaaaatgntn gggggccttg ggtggtggtc tnaaaanacc cctgggggat nttaaacc 900
aaantgaaga agggaaaaat ntttccccnt nttttntttt tttgccccct tgggattggn 960
ttttntttcc

```

970

```

<210> 740
<211> 739
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(739)
<223> n=A,T,C or G

```

```

<400> 740
gntgtcnaaa aagcaggctg gtaccggtcc ggaattcgcg gccgcgtcga cggcccttgg 60
tgccactagt tctttcattc ttcccncca tcaatcagtg aacttttttag cctactcaaa 120
gctttgctcc aatgcatagg atttatgatt gtggggattt ccagataata taaatattca 180
acatgaatat tttaaattaa ggcattgagac atttttccta actgagcata gccatgaacc 240
tctcacgtct gttcctctgt gncagtttgt agcactgaat acagcagccc tcctaaaagt 300
ccaggcagtg cacaggtctt gacatgatga agtgacgtgt tgctatggtg attttgcagc 360
tgcccaaaata gtcaactggt gattttaccc agcaggagat ttttgcaaaa atttcctggg 420
tgagagtga atcaaaactcc tattttgttt ctctcttgca agctgnagtt aanatggatt 480
aatgagtact tttagattaa ttaactctga agagaaaatg ggagaaaagn gaggaagggt 540
gttggcagaa gtcatgtctg gaatccttct gaaggagta ctgacttcac ttgcaaagac 600
aagagactan aagacaatga agttaaactt ggcctgtctn tcatatgata gatgcttgag 660
agtacaggnt cagggaaatt ttaattctgn catacgcata ttggattatg tgggtcatgg 720
ctttgtttgg cncctaacc

```

739

271

<210> 741  
 <211> 1171  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(1171)  
 <223> n=A,T,C or G

<400> 741:  
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 attcgcggcc gcgtcgacgg cccttnntgc cactagtctt ttcattcttc ccccccata 120  
 atcagtgaac tttttagcct actcaaagct ttgctccaat gcataggatt tatgattgtg 180  
 gggattttcca gataatataa atattcaaca tgaatathtt aaattaaggc atgagacatt 240  
 tttcctaact gagcatagcc atgaacctct cacgtctgtt cctctgtgtc agttttagtc 300  
 actgaatata gcagccctcc taaaagtcca ggcagtgcac aggtcttgac atgatgaagt 360  
 gacgtgttgc tatggtgatt ttgcagctgg ccaaatagtc actggttgat tttaccagc 420  
 aggagatttt tgcaaaaatt tcctgggtga gagtgaatc aaactcctat tttgtttctc 480  
 ctctgcaagc tgtagttaag aagggttaa tggagtactt tttagaatt aaattaacct 540  
 cttgaagaa gaaaaaatgg gggaagaaaa aaagtggag ggaaaagggn ttggttttgg 600  
 gccnaaaaaa aagttccaan tttnggcntt ggggaaaaat tccccntttt ccttggnaaa 660  
 aggggggnaa ggttaancct tgggaacctt tttccnncct tttnggccca aaaggggaac 720  
 ccanggggaa agaaccttta ggnaaaaggaa acccatttgg gaangggttt naaaacctt 780  
 ngggcccccg ggccctcttc caanaaggga aaaaaaagg cctggaaaan gtaccagggt 840  
 ttcangggna aaanttaaaa ttcttgacca atancnccat aattgggaat tatggggggg 900  
 ccatgggctt ttggtttggg cncctaaccc cgcnttttaa attcaanna aaaaaagng 960  
 gtttgaaaaa nnaaaanaaaa aaaattnaan ggncccnaaa aaaaaccctg gaaaaccttt 1020  
 ggaaaaaaat tngnnggggg gccntttggt tggggggggt tnaaaaaacc cctnnggggg 1080  
 ttttttaagc ccaaaagggg gggaggggna aaanggtnc cttntttttt ttttnngccc 1140  
 cccttgggga atggnntant tcanggggcc c 1171

<210> 742  
 <211> 739  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(739)  
 <223> n=A,T,C or G

<400> 742  
 gntgtcnaaa aagcaggctg gtaccgggtc ggaattcgcg gccgcgtcga cggcccttgg 60  
 tgccactagt tcttctattc ttcccnccca tcaatcagtg aacttttttag cctactcaaa 120  
 gctttgctcc aatgcatagg atttatgatt gtggggattt ccagataata taaatattca 180  
 acatgaatat ttttaattaa ggcatgagac atttttctta actgagcata gccatgaacc 240  
 tctcacgtct gttcctctgt gncagtttgt agcactgaat acagcagccc tcctaaaagt 300  
 ccaggcagtg cacaggctct gacatgatga agtgacgtgt tgctatggtg attttgcagc 360  
 tggccaaaata gtcactggtt gattttaccc agcaggagat ttttgcaaaa atttcctggg 420  
 tgagagtga atcaaaactcc tattttgttt ctctctgca agctgnagtt aanatggatt 480  
 aatgagtact tttagattaa ttaactctga agagaaaatg ggagaaaagn gaggaagggt 540  
 gttggcagaa gtcattgctg gaatccttct gaaggagta ctgacttcac ttgcaaagac 600  
 aagagactan aagacaatga agttaaaactt ggcctgtctn tcatatgata gatgcttgag 660  
 agtacaggnt cagggaatt ttaattctgn catagcata ttggattatg tgggtcatgg 720  
 ctttgtttgg cncctaacc 739



272

<210> 743  
<211> 610  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(610)  
<223> n=A,T,C or G

<400> 743  
ctgtccttat ttcttttagca aaaatttccc aagagaagaa ttgctgggat aatgcacatt 60  
taaatttttg atagacattc ccaaataaia tacctgtttt tgagaccttt aattcctgtt 120  
gtcaaatgac cctatatatg gagtaataaa cacgatttaa agaaatgagg actaaaaaaa 180  
gattatatat aaccaacat aaaggcaacc tcttaggcgt tgacagaaac tgacaacttt 240  
ttatctgtgg gtgcgatcca ttataagtaa cctgagcacc ttattttttc tttttaaaact 300  
ctaggtagga taccgaggt ccacaaattt ttcataagaa atattttttc tctgccctat 360  
gagattttta aaaatattat actgcttcaa ttgcatcaaa agaaatggac cctaatatct 420  
atgatgaagg atttggagtt agaagacctg agtttcaatt ttggcatggc tgtttgtcta 480  
gctctngat cttggacagg tcaattgact tggcttaatc ttctcatcca tttagnggag 540  
acagcaccac tattcacagg actattgnen gaattaccag acaatagcat agngaaaaat 600  
ataangcctt 610

<210> 744  
<211> 127  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(127)  
<223> n=A,T,C or G

<400> 744  
ttnacctccc tggaccgggc ccccttccc cgggcggntc ccccgggctg caggaattct 60  
gcacgaggga gagagagttt gagagagaga gagagagaga gagagagaga gagananaga 120  
gagagag 127

<210> 745  
<211> 458  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(458)  
<223> n=A,T,C or G

<400> 745  
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ggaagctggg ctacgtcctg ccaggtcag ccttaggtta agggctgcct gggggaggga 120  
acttccctgg ccttcgggtc tctgtgcaact ggggtggctc ctgtggccca gaatgccctg 180  
gagaagggtc ctactggaag cgaagggtga gggcagcagg gcctgaggcg caggagctgg 240  
tggaggctcc cagcacaggc cggcccccga gtcacatcac tgctgatggg ggggggactt 300  
ggggagtttc ccccgagaat gggaggtctc acagtccccg tgctgcaatg ctgtcgggtg 360  
actgngcnng caatgtgctc atggncaact gctttttctc tgtggccccg gccgatttat 420  
ccagcanngc accctcttc tncctcctcg anaaagcc 458

273

<210> 746  
 <211> 893  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(893)  
 <223> n=A,T,C or G

<400> 746  
 aagcaggctg gtaccgggtcc ggaattcgcg gccgcgtcga cgtggggagt tagctctctg 60  
 gaccccgctca tagagtaagt catcgataga gcatttgctt gatggggact tccagaaggc 120  
 canngaaagt cctgccgact tcctggggaa gcccatccgc acgtgggggtg aggggtcccca 180  
 natggaagca gctgtgtatg cagggagggg gcagaggctg ctgccaatgg gcatgtccct 240  
 tacctgaaaag ggccacctct ccaggtgaca tgtcctgggg gagccggggc cgtctgtctc 300  
 ggccagaggg gctcagctca ggccacacca ggcaggggcac ctccaacct ggacagggtg 360  
 ggaccaaggt ggccttgac aaaactctct gtgtttgcc agcacccaat cggacacaga 420  
 gactcaacca caccacagtc acatgggtgc cacacngcag gggtaagga ggcccgccc 480  
 ctccccctca gacgtccctg ggcctctggg agtcagcaag gacgaggacg gcattgccct 540  
 tcgagacagg aaggagtgga cctcctccc gcggcatcca ggctcngctt ctccggagag 600  
 gagagggggc tacttgctgg ataaancggc cggggccaca gagaaaaagc aaggtagacca 660  
 tgagcacctt gcaaacacag tgcacccacc agcatttnag caccngggac tgtgaagacc 720  
 tcccatttct tcggggggaa acncgcccac ngttcccccc accntcacta gtgnattgtg 780  
 acctgggggn cgggccgacc cctgtngctt ggggnagccc tccnccagg tttctnnggc 840  
 ngcccnttaa ngnccctng nttggccctt tggcncctt tncgttttc cca 893

<210> 747  
 <211> 738  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(738)  
 <223> n=A,T,C or G

<400> 747  
 gatatcccgg gaattcgcgg ccgcgtcnac gaagcacaga cctnggccct gctctcatgg 60  
 ggcagactgc catttgtcat tnattactga aggaaggga tcctcagttt gcttgtggac 120  
 atttcaaatt tgaggtgaga gttggataag taagaataaa gctgctcttc aaagagatga 180  
 atatagaaaa agaaacaaga tacagncttg gcagtaaggc tgggaggaag gggaaaagg 240  
 aataaagaat gaaagagtga gaaatgtgag caggagctga acacagaaaa gttcagngac 300  
 agaagcanaa ggaggggaaga agggaggagg gtccctttca cagaggctca cgaggatgct 360  
 ttatgngtgc catgcagtcc atgttcagga tgtctgcttc ttanctctct acttttctaa 420  
 tanaaatttg gatacttact gatcctacat atgtaacagg gagagaagg gaatttcaa 480  
 gcantaaatt gaaaaattgt tcacaatttc attttttaa aaaagggagc taacagaaga 540  
 agaggttaat gtggttaatta taggatgnc cttgcgacac atgaatgnat ctggatcat 600  
 ctgagtgagg ggggagctgt cttcctgacc caaaaggatc ctttcgttan ccngnactta 660  
 ngtcccaaaa cctcaccacc ttggagaaat natttccttt tgggggtntc attaaancct 720  
 tttggncccc gcaaaagc 738

<210> 748  
 <211> 647  
 <212> DNA  
 <213> Homo sapiens

<220>

274.

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(647)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 748

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ctntgtggcg gtggctgtct catttgggtg gacttttttg gtogtaggaa cctggtatng 60
aggctcgagag taagacgggc tattagtagt cgcacgcgag ttatttgtga aaacctggtt 120
agggcctctg tctccgctgc gctcgcttaa attggtatgg ctgcacttgg aaacacggtt 180
ctaacacgcg ttgttagcgc ccttgctagc atgtgaagga cactggccct accaagaaag 240
attcgagtcg ctccttccgg tatcgttcac ggaggcgata ttactcttc ttactacggt 300
tacttcgaga ttgtctgtga agtttaagac tactaaaaag agtattaagc ctatcgggaa 360
ttagctagat cgacacgcta aaaccaaggg caatcggcgg aaatataag gcaccaataa 420
tagggcctac agaaggcccg agggtagac tcacgtttaa taccggccac gggagaaata 480
aaaagataaa gtatacatcg tttagcggtc ctcggaagcc ttcggcttta atgccaagga 540
gtcgggaagca tcgtcggcga gtaataaact ccatcgcgcc gagactatct acgacgccct 600
ccttaanac cgtaaattac tcccggaaag agtatttagg cggctct 647

```

&lt;210&gt; 749

&lt;211&gt; 642

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(642)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 749

```

ctntgtggcg gtgntgtct catttgggtg gacttttttg gtogtaggaa cctggtatgc 60
aggctccgagc agcgtgggct ctgcctgtgg atgttggggg ttggtgtggt gccggttgtt 120
tttggttctg ttgagcgtag tgtgtttgaa ggtagcgtt cgtgtcttgc ttgtggtttg 180
gtgttttagg cgggtgggga ggttgttgtg tagctgttgt atgtcatatt gttggtgttg 240
ctgccctgtg ctgtttgtcc ttggttattg tgggtgttac ccgcctgtg tgggaagtgtt 300
gtggcagggc gggaatttaa gtgggagagt tgtgggacct gtggtgtgtt ttacgttgtt 360
gcttttgtcg tgggcggtg gggcgcgtct gataattaga attggatacg gagtgtataa 420
tacttctagt aaatggggac ctagtgttgc acttcccggg atagggatct atgcgaagtc 480
cttaggatag tctttgataa gtttaacgcc cagcacccta aaattataca cgattagacg 540
cataacgact cctccaggaa agataaagaa tctcacatat agaacgggac ccataacag 600
tcggatagga aacaagagaa ctaattttng ttaaaaagac tt 642

```

&lt;210&gt; 750

&lt;211&gt; 639

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(639)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 750

```

tttgtggcgg tgggtgtctca ttgtgggtga tttttgggtc gtaggtaacc tggatatnag 60
gtatagatgc cgattgggtc cgacgagcgt cagcataaat tcggtagtgtt cgcctttttt 120
agaaggcgt agtactcgga acttcacttc atctcggtag ttacttttgg cgtatatagc 180
cttctccctc gaagactagc cgtcacattc gttccctagg aatcgtttct gccctaaga 240
atccgagagc gagatcccga aactagagga acctagaag agtcgtatct ccacaaggac 300
ccacagtca ttccgggaaa atccctagga ccatacgggt aggattcccc cggaacccgg 360
agcaaagctc atgatttccc acaccgcgag agcgctata accctatccc atttcttcgg 420

```

275

```
gttatcgagg atattacgat caagcogaga gaaccgctag aaccgctttc ttcgctttct 480
cacggaacct ataagtagaa agagaaactc aggtcttaag ggggcgcttc ggctaacgaa 540
acttctactt acgaagagag tatctagaca ttaagtcata aaaatccact acgcacctcg 600
tgtacgatat catcgggagc ggttcataga cgggtgccg 637
```

```
<210> 751
<211> 637
<212> DNA
<213> Homo sapiens
```

```
<220>
<221> misc_feature
<222> (1)...(637)
<223> n=A,T,C or G
```

```
<400> 751
cttttgtggc ggnggtgtct catttgggtg gatttttggg tcgtaggnaa cctggtatng 60
aggcagctct gagccccccc ccccccccc ccccccccc ccccccccta ggnggttggg 120
aanacggttg atacctaaat cgagtnggtt cattaaaaagt agttgattac nccctaaaa 180
aanaanaggg cttcgtcggg anaaatcggt aagganaagt ctttntggca tcataanaat 240
actggctcgg gtcctaanat nttaagngg gtcnccgagg gtnttcatac cgataanaaa 300
cgttttccta tcggcaacgg gcttacctga gggnggactt ctncggngc ggngattnan 360
acgaanacgt agaggattnc cgtacttnt tganatcacn cgtatcatac ttgtaagcat 420
aattntcctg aaaagtgtta taanaatacg cncgcattat cgctttttcg tcctagggat 480
gcttaaatgg cgatactgct atagcgggtg agcgttgggt ctcgagnaan aaagcgtgtc 540
ctaatacgctc taaggnntta agnncgttgg tttaaaaata nccttagaaa cctcgaggcg 600
gatactggtt tntttttaac gaaacaaagc accccnn 637
```

```
<210> 752
<211> 644
<212> DNA
<213> Homo sapiens
```

```
<220>
<221> misc_feature
<222> (1)...(644)
<223> n=A,T,C or G
```

```
<400> 752
tntgtggcgg tgggtgtcat ttgggtggat ttttgggtcg taggaacctg gtatgaggtc 60
ttgcgagttg ttggtgtgtc ctgtcgttcg gtggttccct tttgagttga gtttgcctt 120
tgaggttgtt agctgtgtt cgtttgtgtt cgtgtagtgc tttgggttga gagggttatg 180
gtggtgggta cgggtgtattg tcgcccgtgg tcgcggggtt ggggtggtcg tcggttttgt 240
ggttcatagt agtcttctgc gttcggtggg gcgggttttg gtgagtagtt tcgttcttgg 300
atgtccatt gaccgccat aatctaagta aggttagta gaaacctct cccgatagac 360
acaaccgtcg tccactaaag acctcgctc tgatttttaa aaggaccga aaaacatccc 420
ttcaacggaa aaaacggaaa aaaagtcagc gaattcaaag aagccacggg agagaaaaa 480
gaactaaagt tagtccgtca ttatatgtc cctcgaggga ggaagcggcg gtggcgaaa 540
atgaggcggg aagaagacg acctctatcg gcggttang ccctaaaagg gcgatacctt 600
acgggatgat aaggacccta ggacgcctc ttctcgatc gtcc 644
```

```
<210> 753
<211> 635
<212> DNA
<213> Homo sapiens
```

```
<220>
<221> misc_feature
```

276

<222> (1)...(635)  
 <223> n=A,T,C or G

<400> 753  
 ctttgtggcg gtggtgctca tttgggtgga tttttgggtc gtaggaacct ggtatgaggg 60  
 aatcagctcg accccccccc cccccccct ccgaagcaga gcccaccca aagtccaccg 120  
 actaccggag taaactctcg gagggtagaa taagaaggag taggtcctag ccaatagaag 180  
 tagttccgag ccgttaggac agcggacgga acattnaaga aagagcctat attagggagg 240  
 aagtaacggt cctctttcgg agctctttaa ggggtagtcc cagaacaagg gaagaggacc 300  
 cgtcggctat tgcccgtcga tacgggctct cacgngnagc ctagggttca ggatagggcc 360  
 gctcgtaaaa ttatacgggt tccgagaaac gcttccgtag accgggtcct aaatcgtccg 420  
 gagtattngg agagggatcc ttcggaccct agggacagag agaggagaac ggaggttaca 480  
 ggaggagaac gtntcctcnc tagttttctt tangtcgaaa aatttcttac cgataggggt 540  
 cctagggtcg gngaatttac ggttcgaaaa acggtagtnc ctaangmntg ntattngggg 600  
 tagtatcggg tcgtttacaa ntctccgtc ttntg 635

<210> 754  
 <211> 721  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(721)  
 <223> n=A,T,C or G

<400> 754  
 accggattng ttntcgagcg cgtgactgct aataaaaaag atggantgcc atcttttttt 60  
 ttnccttgct ttatatatcc agcagcaaaa caaaattgtt ctgcngggct ataaaatttg 120  
 gcttgtagt cntgtacaca actcaggagt gtgacacagc taccagcttt cctcctaact 180  
 ctcaaggga gaaaattcaa gttctgtcta ggctcactct gtaaagtggg aaacttgctg 240  
 gttttgtagg ctttttttcc ccttctttcc ctctctcagc ttctccctgc ttctcagaan 300  
 atggagttgt gatgcctgca acttaccaaa tttatctatg aatcagattc cagtgggaga 360  
 ccctaaaagc agagggagaa taaggagttc tcccctatgat ggaaaatata caaagacaag 420  
 gtttcatgga gcaaagaatt ctggctagat ttggtttgta agtggatccc tcccactgc 480  
 gtgtacacct tatctgtctc tttgcttctt ccccaccctc tttccagct ctctctctgt 540  
 ctctctcttg ntcccctgac ccttttttct tcccantgca tacttttttn ttccctttt 600  
 ttaatcttct atantcttaa ncctaccaan gggccctcnt gannaatttn tcaccctga 660  
 ataggggatt cnttangccc tgagaatttc nttatcanaa aaatattttt ttaaagcatt 720  
 a 721

<210> 755  
 <211> 721  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(721)  
 <223> n=A,T,C or G

<400> 755  
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 ttnccttgct ttatatatcc agcagcaaaa caaaattgtt ctgcngggct ataaaatttg 120  
 gcttgtagt cntgtacaca actcaggagt gtgacacagc taccagcttt cctcctaact 180  
 ctcaaggga gaaaattcaa gttctgtcta ggctcactct gtaaagtggg aaacttgctg 240  
 gttttgtagg ctttttttcc ccttctttcc ctctctcagc ttctccctgc ttctcagaan 300  
 atggagttgt gatgcctgca acttaccaaa tttatctatg aatcagattc cagtgggaga 360

277

```

ccccataagc agagggagaa taaggagttc tccccatgat ggaaaatata caaagacaag 420
gtttcatgga gcaaaagaatt ctggctagat ttggtttgta agtggatccc tccccactgc 480
gtgtacactt tatctgtctc ttgtctctt cccacccctc tttccagct ctctctctgt 540
ctctctcttg ntccccctgac ccttttttct tcccantgca tacttttttn ttccctttt 600
ttaatcttct atantcttaa ncctaccaan gggccctont gannaatttn tcacccctga 660
ataggggatt cnttangccc tgagaatttc nttatcanaa aaatattttt ttaaagcatt 720
a

```

```

<210> 756
<211> 873
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(873)
<223> n=A,T,C or G

```

```

<400> 756
ggaagaatac agtaagtttg caaattaaaa tttctctatt tttctgttat ttattcattt 60
ggaaactgtc agcctgtctc ttctactttg ggcaagtga agcaaagacg tccagtccta 120
tcagcaatta ggctgaaagt caacgccaag ctggcgggca agggctgggc tgagtagagg 180
ttccctaggg aggcagaga gagactccca ctcgatactc ccagctcggc aactgcctga 240
atgccaatga gcactcatta taaccogccc tattttatag gatttaattt tacacttcag 300
gcttaaatcag tctgaaagtt aaactgacag tgttaagtta cggaatcaat gacatttagg 360
ctttatgact ttgtagctga atatctatgg gctatatctt cattctaaca gtgatatcct 420
gttcacgaat ctcatctctt ggtgatggca ctttctagtg gagcagtcac ggtaacagtc 480
cacacccatt accatgtggg tgctttacag catactgacg gaaggactga ggagccaccg 540
gagcaggagt tcctctcagg gaggacgctg acacttccac agctgcctan gtatgggcac 600
ctgatgccaa cgaanaaccc aaagcgctct ccttccaga tggaagctgc cccacactgg 660
gctgacagca tctggagctg ctctggctca aatcccgaa tcgcacanct cctancgggg 720
gcgtttanag atcctcnggg ccagctaccg accacttttg acaagggnc ttaggagcga 780
aactagnctg gcgcgttaca cncggatgga acgtcttgga cttgagacct cttgggggan 840
atggcncccc caaataantt gggaaaantn ggg

```

```

<210> 757
<211> 782
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(782)
<223> n=A,T,C or G

```

```

<400> 757
ggcccctcga gggatactct agagcgggccg ccgactagt agctcgtoga cgatatcccg 60
ggatttgaga ccaggagaca gctccagatg ctgtcagccc agtgctgggg gcaggcttcc 120
atctgtgaag tggagaggcg ctttgggctt cttcgttggc atcaggtgcc catacctagg 180
gcagctgtgg aagtgtcagc gtccctccctg agaggaaactc ctgctccggt ggctcctcag 240
tccttccgct agtatgtctgt aaagcaccca catggtaatg ggtgnggact ggtaccatga 300
ctgntccctt aaaagggtggc cttccnaag aaaggagaat tcttggacna gggatttcac 360
ttgnttagaa atgggaaaaa ttaccattta gaattttcgn ttccaaggcn tnaagncccta 420
aaaggccttt gattcccgaa ccttaaccct gggcagttaa ctttcaaac gggataaacc 480
ctgangggga aaatnaaatc ctttaaaaaa gggggggttt naaggagggc tctttggctt 540
tcaggcantt gccaacctgg gaaattcana ggggaagtnt ttttttttgc ctgcctaggg 600
aacctttact taaacnaacc cttgnccccc catttggggt tgactttcan cctaatttgt 660
gaaaggaccg ggccgntttt gntttccttt gncccaaagg naaanaaacg ggtgccantt 720

```

278

cccangggat tanttcccga aaatttggnn aatttttntt tgnaactttt tgggtttttt 780  
cc 782

<210> 758  
<211> 647  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(647)  
<223> n=A,T,C or G

<400> 758  
ntttgtggcg gtggtgtctc atttgggtgg actttttggg tcgtaggaac ctggtatnga 60  
gggaagagcg ccgtcgggcc gagtacagta tggagtagta tagtcttcgc gccttctcgg 120  
gcggcggggc tattctctcc aaaggcagag gtccctagtc gacctcgcct ccctagggtta 180  
ggaacagccg tcgaatattt taggttcgtc gaggctttct tccgagctct acgcctaagt 240  
agctccgcga gcaaagtatc ggtcattttc ccctatccat cactccccta agtacgcctc 300  
attattccgg aaggcaagag gccagcattc ctcccttagag tagagggtag gtacctccgt 360  
cgcggtccgc gaaagggcag agcttcgtgt ctccctccg cagcagctta acggtctacg 420  
taggcgttct cgatcttttc acgggaatcg gggccgggga gggcgccgga aaacgtcgac 480  
gtctcgggtc ccgtcaccgc ccgaacaac tagcggcttt ccgctttcaa ctgaggaacc 540  
ccgcaccctt cattagcgct tacgaaatcg gggangtgat tgcgcccaatt cgttagcctt 600  
cgataattat tctctattag cggtcctatc tcgcgctttc gatttat 647

<210> 759  
<211> 657  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(657)  
<223> n=A,T,C or G

<400> 759  
ctttgtggcg gtggtgtctc atttgggtgg actttttggg tcgtaggaac ctggtatnga 60  
gggctctata gaaagcctct tgtctttaga tacgggcttt ctggtccttc gttctggaag 120  
tgtagtagta ggtactgcgg gaaggcgaag agtcctttca aggacgattt acttaagttg 180  
gcttattcta tagttccttc gggacataag gtcggtacga tctatactgc gtgggaagct 240  
gataggttgg gacttaaggc gaataagaag gaggcggcgg aggtcgcgat taccgcagag 300  
atattattta cggcgccgc gggtaccgcg ggtcatgcgg aaattttctg aggttcttgg 360  
attcctaaga tcgctcccgt cgagtatact agcgacgaac gtaagagtgc cctcacaaga 420  
accggtacaa actcaagaag aagttcccat taagcatcgt aagaaacggt aggacgagga 480  
cggtaagaag taatcggaga aaggatccta gtngttacga agaagcatcg tttagctact 540  
ttgcgctacc gtttatattt agacgtgttc cgtccttctc cgtgtttana aaaaaggtt 600  
attccgacgg gagacttagg cgaatggagg gttccgcggt tganaatcgg ancgggg 657

<210> 760  
<211> 644  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(644)  
<223> n=A,T,C or G

279

<400> 760  
ctttgtggcg gtggtgtctc atttgggtgg actttttggg tcgtaggaac ctggtatgna 60  
ggaaaagaag taagcctcga agcctatctc cgaccgtatt tatttcgcag aagacggaac 120  
tacggacgtc gttaaccccg agtagccccc gtaagaaagg actaaagcga atggaaaagt 180  
cgggaattcc ggcgaggggg cggcgattac tgaaaggagt aagagtaaga ctattgcgat 240  
acttgaggcg ttccctctta aaaggcaccg gaaacactct attaaaaaac acccgaagaa 300  
gaacaactca tgcgatcggc cgtgtgcagc cgtcaatagt aaagagagcc atgaaccatg 360  
ccatcccttag accaattagg atgaagaaga ggaggaagat gaggaccaa ccctaccac 420  
tcggaaaacc ccgcacgagc ctccgaacaa aatccgggaa ttaaaacggc ggcccacttc 480  
cgcaactctcg tagcgcgagc cgaatagaaa accggaaact acagctaaag ggtcctttcc 540  
ggcctgttat ctaccacacc gcaatccgat cctccccccc cctcgtccaa aaaccctaac 600  
ctctgcggca acattagagc agaaggagag ggcgatccct tgan 644

<210> 761  
<211> 647  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(647)  
<223> n=A,T,C or G

<400> 761  
ctttgtggcg gtggtgtctc atttgggtgg actttttggg tcgtaggaac ctggtatnga 60  
ggcgggtact ctctgggata atcggtataa gtgttgtaaa attgggggta agagaaagtt 120  
tcattataag aagtgggaagc acgagccggg gtgttttagtc gttaatatta agaccggttt 180  
ttgtgtgact tatatagctt gcgcgtgggg aggcaataag aaacattgcy ttctgaggcc 240  
ggatgcgggg aaccctcttc ggggtctaga gcgccgcac tcgaaaataa ggactactga 300  
cgccgctcat aacgtactca acaatgagtc ggcctgcatt aagatttcgg cgaagaaccg 360  
tactgcgtct actgatagta tattgcattg atagcggcat gagctttatc acgtgtcgtt 420  
ttcgggttgt aagaagggag ttaagtcgat ctctgaggaa gaagagaccc caaataaaaa 480  
atgactcaaa aaaacctaga agaaacacga cgaaaggaaa aagaacgtta aaactagtag 540  
ctcttcggan gagtagcctt agtagggtaa gtcctccgtg cgtactgtcc taaggtttgg 600  
atagcgcggt tgaatagacg gtcacgcgtc agaaggtaaa aanccgg 647

<210> 762  
<211> 628  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(628)  
<223> n=A,T,C or G

<400> 762  
cattgtgttg ggtcactga gcccactttt ttccagattt tttgtaaaat tgtttcgcat 60  
tgtgtccct ttattcgctt gtattaatat ttgcgtagtg gattaacaa atacttgggtg 120  
ttgactgtca gtcttagagg actgactaga agtagttttc atttggggct caggaaatac 180  
ctactttata ttcttagcta attaggaaag tcatttttca gttaggttgg tgttttgggt 240  
caggcactcg cttagctagat gacctaacat gctacttaat ttctgagtgt ttgtgtccat 300  
ccctgtagga ttgttgcggg gttaaatgaa attgtgtata tttgtaaaagc atttacctca 360  
gtgcccagac tgtgacagag tagattatta ggcttgctct tatttctgtg attaaattta 420  
gtgtcagatt agcaacctat agctaactct aaagctgctg ctgctttctt tgtttagggt 480  
taggaagaaa catgctggac agtttgccaa atgagagtta catgatgtgg cttgtgggaa 540  
cattctaact tggaacttgc ccatttccag gactttgngg ttcanagatt tttggggata 600



280

gatgtaaggg ttaaaaaaaaa cngaaaac

628

&lt;210&gt; 763

&lt;211&gt; 147

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(147)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 763

cattgtgttg gggcagagat aaataattcc tctgaaaagt gttttattgg aatttcaa 60  
gaaaagctaa ctggataact tacagcatgt ttctgccaat aatctcttan aacaggccto 120  
ttttttttat gcacaccacc ttonggc 147

&lt;210&gt; 764

&lt;211&gt; 146

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(146)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 764

cattgtgttg ggtatgtttt ttgaaggcag gtggacagga ttgctgatg ggtaaatggc 60  
agagttaggg ggactgttag aacagagaaa.ganatcatgg ggttgggttt gagtctgatg 120  
nnnaactgggt gccgnntgct cagtat 146

&lt;210&gt; 765

&lt;211&gt; 129

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(129)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 765

tncncgattc gntnctagcg tntacactna tgtcttggtta ccgagctcgg atccactagt 60  
ccagtgtggg nggaattcca ttgtgttggg gcaggaggng ctttgngtac ngtgcggctg 120  
nagaggcgg 129

&lt;210&gt; 766

&lt;211&gt; 175

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(175)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 766

281

```

cattgtgttg ggcctagtcc gaatactttt agtaacttca gacagatctc ctcactctctt 60
totggggctt ggntttttctc ctttgtanaa tgatgccttt ctgtgggttt gtcattttcta 120
acattctgtg ngtgatgagg tgttatattcg angantcteta tcnccanagt actct 175

```

```

<210> 767
<211> 602
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(602)
<223> n=A,T,C or G

```

```

<400> 767
nnntttaaaa nctgtntctcc ccgcggtggc ggccgctcta gaactagtgg atcctttcca 60
cctggtttgt tttcagtgtt taatcctatt agtatcagca ggatataggt caggatatca 120
ggtgcagaac ctgtggaatc agccaatttg gcttgctcat ttactttaat aagggtcccat 180
aatgagtgtg agtacaaagt tcaagccctg ttgagggtct gcattaaact ctcagaagta 240
tttagagtgt gccaggagcc gcgaagggtc gggtcgggtg gtggcgggaa ctgtattaga 300
gtgctaggca cggcgcgaca aagtctgtcc aacccaaaac ggtgctgagg cgttgggtgt 360
gagctccagt actcagaaaa gcctctcagc aggtactcaa cagatcctca ggggcttggg 420
ggcccagcac tggcagtgtg ggcatgaaag acataaaagg gcactacctg tgggtatttt 480
ctgttctcca aggaggaagt agcaaaaatt aggacgtgtg aatatcctat gttgtagcaa 540
tcccagaaca actgatgttc aacaaatacc acacaaaaca aattttttaa aatttaactct 600
ta 602

```

```

<210> 768
<211> 671
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(671)
<223> n=A,T,C or G

```

```

<400> 768
tccaccgcgg tggcggcgcg tctagactag tggatccact agtccagtgt ggggtgggaat 60
tcgcggcncg cgtcgacaaa aatactgcta aagtaatatt tttatagatg actatttgcc 120
ttggggccag gaaaagcagc tggagtattt cacttagtac catttttaca tactaacttt 180
gccttttcca tgcttgcttg atgcggttgc cagcactgaa gaacagtttc aattgctagc 240
caaccagaga gcatgatcaa accaaacaag ttccctgttt caggaaaaac aggttttagg 300
taactgaagg gttaccagtt actgattcca caatcttctc tgtaaaanat ttctgcctat 360
tatgcagact gggcggtctt aaanntggta aaactatnaa ataccatac aatattttta 420
nggggcccen ttatnaagct tttcaggcct tcccctttcc atagcatttg tgggatacaa 480
gaaaccttta aacagcaacn agctatcnag gcccaaaagg aaagtaattn tgatttttta 540
nagattccgn aacgaaaaaa tggctgggtt caaatacnac cttcttttta aaatggnttc 600
cttattaaac nttttttttt ttttaattta ccccatggtc ntgatnttng ngcttccgcc 660
canaaaatng n 671

```

```

<210> 769
<211> 877
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature

```

282

&lt;222&gt; (1)...(877)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 769

```

aaagctggag ctccccgcgg tggcgccgcg tctagaacta gtggatccac tagtccanng 60
ngggggaatt cgcgccgcg tgcacctcta tacctttgnt catgcagctt cctctgactg 120
ggtttggtct tcaacttggt aacctctctt ttacttaagc acaccttgaa cattccctcc 180
ttccccattt ccccgagng cccctaattg acatacttct gaataacaca ggtggtattc 240
cttccttggt ggaacctcct ggaggaagag acagatgatt acaaatcct tccatcaacc 300
cctttgacca tgacatcaac agtgctccaa attatggggt accgtattag cctatgtcta 360
tcttgatcag aatccttacc tcggtgtatt gaaattatct atttcgtgcc tgcctcttta 420
aagtcagggt ttgccttacc tattgtctaa caccatgcag taggtaacat gcagtaggaa 480
acatggcatt aaattatttg ggttcaaacc ccagttatgg tgtgtaaatg cctaccaggc 540
cgtgaggcac ctgctaagca ggttgacgc atcatttgaa ttcacaccac ccttttgcaa 600
tagaacagat aggcaacaga ggctcatttg ggctaaagga tttgatggag gggaagtgcc 660
aggattccca ccaaggcctc anggccagg tccanggacc atgtctgttg tgacaactgg 720
agtgcatctc atatccctn ctctgngggg naaggtccct cncgnggaga acnnttaaaa 780
caatcatntc tnggggntt aatgcttctt nccccagtgt ggtncactgc ngccacgagt 840
cccancact agtcccangt ctgtcatgaa ccancec 877

```

&lt;210&gt; 770

&lt;211&gt; 874

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(874)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 770

```

ctggntcccc cgcggtggcg gccgctctag aactagtgga tccactagtc cagtgtggtg 60
gaattcgcg cgcgctcgac cttttcaaag gttaacttat ttaattatca canngcaac 120
ccgatgagta gtaacagta ttttactgat aggtaatcta aagaaggagg ctaaataaat 180
tgcccaattt cgaacagta gaggaagaat taggattgaa acacatatag tggcttcaga 240
atctgttaacc ctacagatgc cactactact tctttcagaa taccctttgc ctatctattc 300
tgttcctatg tcatcaaatt atacttactt taaaaagtat ttgtctttat tattttttaa 360
aaaacacagg gaagtatttc tgatcagggg cagtattggt tctgaaagac aagccagtgt 420
ttttgagggt ttctcccttg ccagtttttc tatgctgggt tattcaagtc ctaagaattg 480
tgtagctatt acagaaccgc tttagcaaat gtgttccatt aatcaagggt atttataaca 540
aaatttcac caagtttgga gtgctctgaa aacatagcca aaatgttcgc agggctctacc 600
cctctcgtgt gtcccttttt tttagctatt tcagaagcac actggtgcaa tattttacga 660
aatgagtttc ttccctttac ctctgcatcc tctaagaaaa aatcattgnt gttttatgaa 720
natgaanatc ctgctatttc atatcttgat tggagctgct taattaaatg accattttta 780
aatttgtttt gattccnngc aaaaaaagtt tnttnttgga tgtagggggc tcnnaaagnc 840
caaaaccccc caaaattttt nnttggaac ccna 874

```

&lt;210&gt; 771

&lt;211&gt; 156

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(156)

&lt;223&gt; n=A,T,C or G

&lt;400&gt; 771

283

```

ttaaaaaanct ggnctccccg cgggtggcggc cgetctagaa ctagtggatc cactagtcca 60
gtgtgtgtgga attcgcggcc gcgtcgaccg cgagcggtcg cccttttttt ttttttttn 120
ngtttttttg aanaattcat tgggtattta ttattc 156

```

```

<210> 772
<211> 586
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(586)
<223> n=A,T,C or G

```

```

<400> 772
ncaanctggg tccaccgcg gtggcgccg ctctagacta gtggatccac tagtccagt 60
tgggtgaatt cgcgccgcg tgcgtcaca agtgcgcaca agtccngnat ttattttatc 120
tccagatatg aaacttacc ccagctatgg tcttctatit gttatttaat ttctaggcca 180
atTTTTtcca cttgaatgtc agtattttta ttcaaagtca ccttgtccaa ataccaagtc 240
atcaacttac cctcaaatta tatcctcatt cagaaaatct acatctatta atggtagcta 300
ttttatccct gccccctgct ttttcttttt atatttaatt aatttgntca tccagcaaat 360
gcttattgag caggtattgt aggcataaca attctanact ttaaggggac acagnttgca 420
aaacaaaatc ctgccttgna tggatactta tgnnatggng ggatacagac aatcaacata 480
atgangngca tcatatataa tggttagnan aatgataagg gnttttgga aaaaaatgca 540
ccanccaan anggattggg aagtggangg ganggtcang ggangg 586

```

```

<210> 773
<211> 2983
<212> DNA
<213> Homo sapiens

```

```

<400> 773
agagatagag tcttccttgg cattgcagga gagaatctga agggatgatg gatgcatcaa 60
aagagctgca agttctccac attgacttct tgaatcagga caacgcggtt tctcaccaca 120
catgggagtt ccaaacgagc agtctgtgt tccggcgagg acaggtgttt cacctgcggc 180
tggtgctgaa ccagccccta caatcctacc accaactgaa actggaattc agcacagggc 240
cgaatcctag catcgccaaa cacaccctgg tgggtgctga cccgaggacg ccctcagacc 300
actacaactg gcaggcaacc cttcaaaatg agtctggcaa agaggtcaca gtggctgtca 360
ccagttcccc caatgccatc ctgggcaagt accaactaaa cgtgaaaact ggaaaccaca 420
tccttaagtc tgaagaaaac atcctatacc ttctcttcaa cccatggtgt aaagaggaca 480
tggttttcat gcctgatgag gacgagcgca aagagtacat cctcaatgac acgggctgcc 540
attacgtggg ggctgccaga agtatcaaat gcaaaccctg gaactttggt cagtttgaga 600
aaaatgtcct ggactgtgc atttccctgc tgactgagag ctccctcaag cccacagata 660
ggagggaccc cgtgctggtg tgcagggcca tgtgtgctat gatgagcttt gagaaaggcc 720
aggcgctgct cattgggaat tggactgggg actatgaagg tggcacagcc ccatacaagt 780
ggacaggcag tgccccgac ctgcagcagt actacaacac gaagcaggct gtgtgctttg 840
gccagtgtgt ggtgtttgct gggatcctga ctacagtgt gagagcgttg ggcaccccag 900
cacgcagtgt gacaggcttc gattcagctc acgacacaga aaggaaacct acggtggaca 960
cctatgtgaa tgagaatggc aagaaaatca ccagtatgac ccacgactct gtctggaatt 1020
tccatgtgtg gacggatgcc tggatgaagc gaccgatct gcccaagggc tacgacggct 1080
ggcaggctgt ggacgcaacg ccgcaggagc gaagccaggg tgtcttctgc tgtgggccat 1140
caccactgac cgccatccgc aaaggtgaca tctttattgt ctatgacac agattcgtct 1200
tctcagaagt gaatggtgac aggcctcatc ggttggtgaa gatggtgaat gggcaggagg 1260
agttacacgt aatttcaatg gagaccacaa gcatcgggaa aaacatcagc accaaggcag 1320
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&lt;210&gt; 774

&lt;211&gt; 3064

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 774

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&lt;211&gt; 684

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 775

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      115             120             125
Ser Glu Glu Asn Ile Leu Tyr Leu Leu Phe Asn Pro Trp Cys Lys Glu
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Asp Met Val Phe Met Pro Asp Glu Asp Glu Arg Lys Glu Tyr Ile Leu
      145             150             155             160
Asn Asp Thr Gly Cys His Tyr Val Gly Ala Ala Arg Ser Ile Lys Cys
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<210> 776  
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 <212> PRT  
 <213> Homo sapiens

<400> 776  
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 Gly Pro Asn Pro Ser Ile Ala Lys His Thr Leu Val Val Leu Asp Pro  
 65 70 75 80  
 Arg Thr Pro Ser Asp His Tyr Asn Trp Gln Ala Thr Leu Gln Asn Glu  
 85 90 95  
 Ser Gly Lys Glu Val Thr Val Ala Val Thr Ser Ser Pro Asn Ala Ile  
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 Ser Glu Glu Asn Ile Leu Tyr Leu Leu Phe Asn Pro Trp Cys Lys Glu  
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 Gly Asp Ile Phe Ile Val Tyr Asp Thr Arg Phe Val Phe Ser Glu Val  
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&lt;211&gt; 5668

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 777

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<212> PRT
<213> Homo sapiens
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&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

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Lys	Ile	Pro	Ile	Val	Cys	Phe	Ala	Gln	Gly	Gly	Gly	Lys	Glu	Thr	Leu	
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Tyr Ser Gly Arg Val Ile Phe Cys Leu Asp Tyr Ile Ile Phe Thr Leu
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Arg Leu Ile His Ile Phe Thr Val Ser Arg Asn Leu Gly Pro Lys Ile
      835      840      845
Ile Met Leu Gln Arg Met Leu Ile Asp Val Phe Phe Phe Leu Phe Leu
      850      855      860
Phe Ala Xaa Trp Met Val Ala Phe Gly Val Ala Arg Gln Gly Ile Leu
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Glu Pro Tyr Leu Ala Met Phe Gly Gln Val Pro Ser Asp Val Asp Gly
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Thr Thr Tyr Asp Phe Ala His Cys Thr Phe Thr Gly Asn Glu Ser Lys
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Pro Leu Cys Val Glu Leu Asp Glu His Asn Leu Pro Arg Phe Pro Glu
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Trp Ile Thr Ile Pro Leu Val Cys Ile Tyr Met Leu Ser Thr Asn Ile
945      950      955      960
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298

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<213> Homo sapiens

<400> 796  
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<210> 797

299

<211> 45  
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 <213> Homo sapiens

<400> 797  
 aacgacctca tgctcatcaa gttggacgaa tccgtgtccg agtct 45

<210> 798  
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 <212> DNA  
 <213> Homo sapiens

<400> 798  
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<210> 799  
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 <212> PRT  
 <213> Homo sapiens

<400> 799  
 Glu Pro Gly Ser Gln Met Val Glu Ala Ser Leu Ser Val Arg His  
                   5                  10                  15

<210> 800  
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 <212> PRT  
 <213> Homo sapiens

<400> 800  
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                   5                  10                  15

<210> 801  
 <211> 15  
 <212> PRT  
 <213> Homo sapiens

<400> 801  
 Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met  
                   5                  10                  15

<210> 802  
 <211> 15  
 <212> PRT  
 <213> Homo sapiens

<400> 802  
 Tyr Thr Ile Gly Leu Gly Leu His Ser Leu Glu Ala Asp Gln Glu  
                   5                  10                  15

<210> 803  
 <211> 14  
 <212> PRT

300

&lt;213&gt; Homo sapiens

&lt;400&gt; 803

Phe Gln Asn Ser Tyr Thr Ile Gly Leu Gly Leu His Ser Leu  
5 10

&lt;210&gt; 804

&lt;211&gt; 15

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 804

Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu  
5 10 15

&lt;210&gt; 805

&lt;211&gt; 15

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 805

His Pro Gln Trp Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser  
5 10 15

&lt;210&gt; 806

&lt;211&gt; 15

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 806

Ser Gly Val Leu Val His Pro Gln Trp Val Leu Ser Ala Ala His  
5 10 15

&lt;210&gt; 807

&lt;211&gt; 15

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 807

Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp Val  
5 10 15

&lt;210&gt; 808

&lt;211&gt; 15

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 808

Ala Leu Val Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val  
5 10 15

&lt;210&gt; 809

301

<211> 17  
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<213> Homo sapiens

<400> 809  
Ser Gln Pro Trp Gln Ala Ala Leu Val Met Glu Asn Glu Leu Phe Cys  
5 10 15

Ser

<210> 810  
<211> 15  
<212> PRT  
<213> Homo sapiens

<400> 810  
Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly Asn Ser Cys Leu  
5 10 15

<210> 811  
<211> 15  
<212> PRT  
<213> Homo sapiens

<400> 811  
Ser Val Ser Glu Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser  
5 10 15

<210> 812  
<211> 15  
<212> PRT  
<213> Homo sapiens

<400> 812  
Ile Lys Leu Asp Glu Ser Val Ser Glu Ser Asp Thr Ile Arg Ser  
5 10 15

<210> 813  
<211> 15  
<212> PRT  
<213> Homo sapiens

<400> 813  
Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser  
5 10 15

<210> 814  
<211> 15  
<212> PRT  
<213> Homo sapiens

<400> 814

302

Arg Pro Leu Leu Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu  
                   5  10  15

&lt;210&gt; 815

&lt;211&gt; 35

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; PCR primer

&lt;400&gt; 815

ggaccagcat atgaggaaca gaaggaatga cactc 35

&lt;210&gt; 816

&lt;211&gt; 29

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; PCR primer

&lt;400&gt; 816

ccgctcgagt ccacccaag cttcacagg 29

&lt;210&gt; 817

&lt;211&gt; 1959

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 817

atgaggaaca gaaggaatga cactctggac agcaccggga ccctgtactc cagcgcgtct 60  
 cggagcacag acttgtctta cagtgaagc gacttggtga attttattca agcaaatttt 120  
 aagaaacgag aatgtgtctt ctttaccaaa gattccaagg ccacggagaa tgtgtgcaag 180  
 tgtggctatg cccagagcca gcacatggaa ggcaccaga tcaaccaaag tgagaaatgg 240  
 aactacaaga aacacaccaa ggaatttcct accgacgcct ttggggatat tcagtttgag 300  
 aactgggga agaaagggaa gtatatacgt ctgtcctgcy acacggacgc ggaaatcctt 360  
 tacgagctgc tgaccagca ctggcacctg aaaacacca acctgggtcat ttctgtgacc 420  
 gggggcgcca agaacttcgc cctgaagccg cgcctgcgca agatcttcag ccggtcctc 480  
 tacatcgcg agtccaaagg tgcttggtt ctcacgggag gcaccatta tggcctgatg 540  
 aagtacatcg gggaggtggt gagagataac accatcagca ggagttcaga ggagaatatt 600  
 gtggccattg gcatagcagc ttggggcatg gtctccaacc gggacaccct catcaggaat 660  
 tgcgatgctg agggctattt tttagcccag taccttatgg atgacttcac aagagatcca 720  
 ctgtatatcc tggacaacaa ccacacacat ttgtgctcgc tggacaatgg ctgtcatgga 780  
 catcccactg tgaagcaaa gctccggaat cagctagaga agtatatctc tgagcgcact 840  
 attcaagatt ccaactatgg tggcaagatc ccatttgtgt gttttgcca aggaggtgga 900  
 aaagagactt tgaagccat caatacctcc atcaaaaata aaattccttg tgtggtggtg 960  
 gaaggctcgg gccagatcgc tgatgtgatc gctagcctgg tggaggtgga ggatgccctg 1020  
 acatcttctg ccgtcaagga gaagctgggt cgctttttac cccgcacggt gtcccggtg 1080  
 cctgaggagg agactgagag ttggatcaaa tggctcaaag aaattctcga atgttctcac 1140  
 ctattaaacag ttattaaat ggaagaagct ggggatgaaa ttgtgagcaa tgccatctcc 1200  
 tacgtcttat acaaagcctt cagcaccagt gagcaagaca aggataactg gaatgggcag 1260  
 ctgaagcttc tgctggagtg gaaccagctg gacttagcca atgatgagat tttaccaaat 1320  
 gaccgccgat gggagtctgc tgaccttcaa gaagtcagt ttacggctct cataaaggac 1380  
 agacccaagt ttgtccgcct cttctggag aatggcttga acctacggaa gtttctcacc 1440  
 catgatgtcc tcaactgaact cttctccaac cacttcagca cgcttgtgta ccggaatctg 1500

303

cagatcgcca agaattccta taatgatgcc ctctcacgt ttgtctggaa actggttgcg 1560  
 aacttccgaa gaggcttccg gaaggaagac agaaatggcc gggacgagat ggacatagaa 1620  
 ctccaagacg tgtctcctat tactcggcac cccctgcaag ctctcttcat ctgggccatt 1680  
 cttcagaata agaaggaact ctccaaagtc atttgggagc agaccagggg ctgcactctg 1740  
 gcagccctgg gagccagcaa gcttctgaag actctggcca aagtgaagaa cgacatcaat 1800  
 gctgctgggg agtccgagga gctggctaag gactacgaga cccgggctgt tgagctgttc 1860  
 actgagtgtt acagcagcga tgaagacttg gcagaacagc tgctgggtcta ttctgtgaa 1920  
 gcttgggggtg gactcgagca ccaccaccac caccactga 1959

&lt;210&gt; 818

&lt;211&gt; 652

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 818

Met	Arg	Asn	Arg	Arg	Asn	Asp	Thr	Leu	Asp	Ser	Thr	Arg	Thr	Leu	Tyr
				5					10					15	
Ser	Ser	Ala	Ser	Arg	Ser	Thr	Asp	Leu	Ser	Tyr	Ser	Glu	Ser	Asp	Leu
				20				25					30		
Val	Asn	Phe	Ile	Gln	Ala	Asn	Phe	Lys	Lys	Arg	Glu	Cys	Val	Phe	Phe
		35					40					45			
Thr	Lys	Asp	Ser	Lys	Ala	Thr	Glu	Asn	Val	Cys	Lys	Cys	Gly	Tyr	Ala
		50					55				60				
Gln	Ser	Gln	His	Met	Glu	Gly	Thr	Gln	Ile	Asn	Gln	Ser	Glu	Lys	Trp
		65			70					75					80
Asn	Tyr	Lys	Lys	His	Thr	Lys	Glu	Phe	Pro	Thr	Asp	Ala	Phe	Gly	Asp
				85					90					95	
Ile	Gln	Phe	Glu	Thr	Leu	Gly	Lys	Lys	Gly	Lys	Tyr	Ile	Arg	Leu	Ser
			100					105					110		
Cys	Asp	Thr	Asp	Ala	Glu	Ile	Leu	Tyr	Glu	Leu	Leu	Thr	Gln	His	Trp
		115					120					125			
His	Leu	Lys	Thr	Pro	Asn	Leu	Val	Ile	Ser	Val	Thr	Gly	Gly	Ala	Lys
		130				135					140				
Asn	Phe	Ala	Leu	Lys	Pro	Arg	Met	Arg	Lys	Ile	Phe	Ser	Arg	Leu	Ile
		145			150				155					160	
Tyr	Ile	Ala	Gln	Ser	Lys	Gly	Ala	Trp	Ile	Leu	Thr	Gly	Gly	Thr	His
			165					170						175	
Tyr	Gly	Leu	Met	Lys	Tyr	Ile	Gly	Glu	Val	Val	Arg	Asp	Asn	Thr	Ile
		180					185					190			
Ser	Arg	Ser	Ser	Glu	Glu	Asn	Ile	Val	Ala	Ile	Gly	Ile	Ala	Ala	Trp
		195				200					205				
Gly	Met	Val	Ser	Asn	Arg	Asp	Thr	Leu	Ile	Arg	Asn	Cys	Asp	Ala	Glu
		210				215					220				
Gly	Tyr	Phe	Leu	Ala	Gln	Tyr	Leu	Met	Asp	Asp	Phe	Thr	Arg	Asp	Pro
		225			230				235					240	
Leu	Tyr	Ile	Leu	Asp	Asn	Asn	His	Thr	His	Leu	Leu	Leu	Val	Asp	Asn
			245					250						255	
Gly	Cys	His	Gly	His	Pro	Thr	Val	Glu	Ala	Lys	Leu	Arg	Asn	Gln	Leu
		260						265					270		
Glu	Lys	Tyr	Ile	Ser	Glu	Arg	Thr	Ile	Gln	Asp	Ser	Asn	Tyr	Gly	Gly
		275					280					285			
Lys	Ile	Pro	Ile	Val	Cys	Phe	Ala	Gln	Gly	Gly	Gly	Lys	Glu	Thr	Leu
		290				295					300				
Lys	Ala	Ile	Asn	Thr	Ser	Ile	Lys	Asn	Lys	Ile	Pro	Cys	Val	Val	Val
		305				310				315				320	
Glu	Gly	Ser	Gly	Gln	Ile	Ala	Asp	Val	Ile	Ala	Ser	Leu	Val	Glu	Val
			325					330						335	
Glu	Asp	Ala	Leu	Thr	Ser	Ser	Ala	Val	Lys	Glu	Lys	Leu	Val	Arg	Phe



304

```

      340      345      350
Leu Pro Arg Thr Val Ser Arg Leu Pro Glu Glu Glu Thr Glu Ser Trp
      355      360      365
Ile Lys Trp Leu Lys Glu Ile Leu Glu Cys Ser His Leu Leu Thr Val
      370      375      380
Ile Lys Met Glu Glu Ala Gly Asp Glu Ile Val Ser Asn Ala Ile Ser
385      390      395      400
Tyr Ala Leu Tyr Lys Ala Phe Ser Thr Ser Glu Gln Asp Lys Asp Asn
      405      410      415
Trp Asn Gly Gln Leu Lys Leu Leu Leu Glu Trp Asn Gln Leu Asp Leu
      420      425      430
Ala Asn Asp Glu Ile Phe Thr Asn Asp Arg Arg Trp Glu Ser Ala Asp
      435      440      445
Leu Gln Glu Val Met Phe Thr Ala Leu Ile Lys Asp Arg Pro Lys Phe
      450      455      460
Val Arg Leu Phe Leu Glu Asn Gly Leu Asn Leu Arg Lys Phe Leu Thr
465      470      475      480
His Asp Val Leu Thr Glu Leu Phe Ser Asn His Phe Ser Thr Leu Val
      485      490      495
Tyr Arg Asn Leu Gln Ile Ala Lys Asn Ser Tyr Asn Asp Ala Leu Leu
      500      505      510
Thr Phe Val Trp Lys Leu Val Ala Asn Phe Arg Arg Gly Phe Arg Lys
      515      520      525
Glu Asp Arg Asn Gly Arg Asp Glu Met Asp Ile Glu Leu His Asp Val
      530      535      540
Ser Pro Ile Thr Arg His Pro Leu Gln Ala Leu Phe Ile Trp Ala Ile
545      550      555      560
Leu Gln Asn Lys Lys Glu Leu Ser Lys Val Ile Trp Glu Gln Thr Arg
      565      570      575
Gly Cys Thr Leu Ala Ala Leu Gly Ala Ser Lys Leu Leu Lys Thr Leu
      580      585      590
Ala Lys Val Lys Asn Asp Ile Asn Ala Ala Gly Glu Ser Glu Glu Leu
      595      600      605
Ala Asn Glu Tyr Glu Thr Arg Ala Val Glu Leu Phe Thr Glu Cys Tyr
      610      615      620
Ser Ser Asp Glu Asp Leu Ala Glu Gln Leu Leu Val Tyr Ser Cys Glu
625      630      635      640
Ala Trp Gly Gly Leu Glu His His His His His His
      645      650

```

&lt;210&gt; 819

&lt;211&gt; 132

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 819

```

Thr Ala Ala Ser Asp Asn Phe Gln Leu Ser Gln Gly Gly Gln Gly Phe
1      5      10      15
Ala Ile Pro Ile Gly Gln Ala Met Ala Ile Ala Gly Gln Ile Arg Ser
      20      25      30
Gly Gly Gly Ser Pro Thr Val His Ile Gly Pro Thr Ala Phe Leu Gly
      35      40      45
Leu Gly Val Val Asp Asn Asn Gly Asn Gly Ala Arg Val Gln Arg Val
      50      55      60
Val Gly Ser Ala Pro Ala Ala Ser Leu Gly Ile Ser Thr Gly Asp Val
65      70      75      80
Ile Thr Ala Val Asp Gly Ala Pro Ile Asn Ser Ala Thr Ala Met Ala

```

305

[illegible]

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<210> 820
<211> 36
<212> DNA
<213> Artificial Sequence
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<220>  
<223> PCR primer

<400> 820  
ggggaattca tgatccggga gaaatttgcc cactgc 36

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<210> 821
<211> 33
<212> DNA
<213> Artificial Sequence
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<220>  
<223> PCR primer

<400> 821  
gggctcgagt caggagtttg agaccagcct ggc 33

```
<210> 822
<211> 675
<212> DNA
<213> Homo sapiens
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<400> 822						
atgcacacacc	atcaccatca	cacggccgcg	tccgataact	tccagctgtc	ccagggtggg	60
cagggtattcg	ccattccgat	cgggcaggcg	atggcgatcg	cgggccagat	caagcttccc	120
accgttcata	tcgggcctac	cgcttctctc	ggctttgggtg	ttgtcgacaa	caacggcaac	180
ggcgacacgag	tccaaacgcg	gtctgggagc	gctccggcgg	caagtctcgg	catctccacc	240
ggcgacgtga	tcaccgcggt	cgacggcgct	ccgatcaact	cggccaccgc	gatggcggac	300
gcgcttaacg	ggcatcatcc	cggtgacgtc	atctcggtga	cctggcaaac	caagtccggc	360
ggcacacgtga	cagggaacgt	gacattggcc	gagggacccc	cggccgaatt	catgatccg	420
gagaaattga	cccactgcac	cgtgctaacc	attgcacaca	gattgaacac	catatttcag	480
agcgacaaga	taatgtttt	agattcagga	agactgaaag	aatatgatga	gccgtatgtt	540
ttgctgcaaa	ataaagagag	cctattttac	aagatgggtc	aacaactggg	caaggcagaa	600
gcgctgcgcc	tcactgaaac	agcaaaacag	agatgggggt	tcaccatgtt	ggccaggctg	660
gtctcaaatc	cctga					675

```
<210> 823
<211> 291
<212> DNA
<213> Homo sapiens
```

306

&lt;400&gt; 823

```

atggggatcc gggagaaatt tgccactgc accgtgctaa ccattgcaca cagattgaac 60
accattattg acagcgacaa gataatgggt ttagattcag gaagactgaa agaatatgat 120
gagccgtatg ttttgctgca aaataaagag agcctatattt acaagatggt gcaacaactg 180
ggcaaggcag aagccgctgc cctcactgaa acagcaaaac agagatgggg tttcaccatg 240
ttggccaggc tgggtctcaa ctcctcgcag caccaccacc accaccactg a 291

```

&lt;210&gt; 824

&lt;211&gt; 1074

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 824

```

atgtcagcca ttgagagggt gtcagaggca atcgtcagca tccgaagaat ccagacccttt. 60
ttgctacttg atgagatata acagcgcaac cgtcagctgc cgtcagatgg taaaaagatg 120
gtgcatgtgc aggatatttac tgctttttgg gataaggcat cagagacccc aactctacaa 180
ggccttttct tttactgtcag acctggcgaa ttgttagctg tggctggccc cgtggggagca 240
gggaagtcac cactgttaag tgccgtgctc ggggaattgg cccaagtca cgggctgggc 300
agcgtgcatg gaagaattgc ctatgtgtct cagcagccct ggggtgttctc gggaactctg 360
aggagtaata ttttatttgg gaagaaatac gaaaaggaaac gatatgaaaa agtcataaag 420
gcttgtgctc tgaaaaagga tttacagctg ttggaggatg gtgatctgac tgtgatagga 480
gatcggggaa ccacgctgag tggagggcag aaagcacggg taaaccttgc aagagcagtg 540
tatcaagatg ctgacatcta tctcctggac gatcctctca gtgcagtaga tgcggaagtt 600
agcagacact gtctcgaact gtgtatttgc caaattttgc atgagaagat cacaatttta 660
gtgactcacc agttgcagta cctcaaagct gcaagtcaga ttctgatatt gaaagatggt 720
aaaatggtgc agaaggggac ttacactgag ttctataaat ctggtataga ttttggtctc 780
cttttaaaga aggataatga ggaaagtga caacctccag ttccaggaac tcccacacta 840
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aaagatggtg ctctggagag ccaagataca gagaatgtcc cagttacact atcagaggag 960
aaccgttctg aaggaaaagt tggttttcag gcctataaga attacttcag agctggtgct 1020
cactggattg tcttcatttt ccttatttct gagcaccacc accaccacca ctga 1074

```

&lt;210&gt; 825

&lt;211&gt; 224

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 825

```

Met His His His His His His Thr Ala Ala Ser Asp Asn Phe Gln Leu
      5      10      15
Ser Gln Gly Gly Gln Gly Phe Ala Ile Pro Ile Gly Gln Ala Met Ala
      20      25      30
Ile Ala Gly Gln Ile Lys Leu Pro Thr Val His Ile Gly Pro Thr Ala
      35      40      45
Phe Leu Gly Leu Gly Val Val Asp Asn Asn Gly Asn Gly Ala Arg Val
      50      55      60
Gln Arg Val Val Gly Ser Ala Pro Ala Ala Ser Leu Gly Ile Ser Thr
      65      70      75      80
Gly Asp Val Ile Thr Ala Val Asp Gly Ala Pro Ile Asn Ser Ala Thr
      85      90      95
Ala Met Ala Asp Ala Leu Asn Gly His His Pro Gly Asp Val Ile Ser
      100     105     110
Val Thr Trp Gln Thr Lys Ser Gly Gly Thr Arg Thr Gly Asn Val Thr
      115     120     125
Leu Ala Glu Gly Pro Pro Ala Glu Phe Met Ile Arg Glu Lys Phe Ala
      130     135     140
His Cys Thr Val Leu Thr Ile Ala His Arg Leu Asn Thr Ile Ile Asp

```

307

145                      150                      155                      160  
 Ser Asp Lys Ile Met Val Leu Asp Ser Gly Arg Leu Lys Glu Tyr Asp  
                                  165                      170                      175  
 Glu Pro Tyr Val Leu Leu Gln Asn Lys Glu Ser Leu Phe Tyr Lys Met  
                                  180                      185                      190  
 Val Gln Gln Leu Gly Lys Ala Glu Ala Ala Ala Leu Thr Glu Thr Ala  
                                  195                      200                      205  
 Lys Gln Arg Trp Gly Phe Thr Met Leu Ala Arg Leu Val Ser Asn Ser  
                                  210                      215                      220

&lt;210&gt; 826

&lt;211&gt; 357

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 826

Met Ser Ala Ile Glu Arg Val Ser Glu Ala Ile Val Ser Ile Arg Arg  
                                  5                      10                      15  
 Ile Gln Thr Phe Leu Leu Leu Asp Glu Ile Ser Gln Arg Asn Arg Gln  
                                  20                      25                      30  
 Leu Pro Ser Asp Gly Lys Lys Met Val His Val Gln Asp Phe Thr Ala  
                                  35                      40                      45  
 Phe Trp Asp Lys Ala Ser Glu Thr Pro Thr Leu Gln Gly Leu Ser Phe  
                                  50                      55                      60  
 Thr Val Arg Pro Gly Glu Leu Leu Ala Val Val Gly Pro Val Gly Ala  
                                  65                      70                      75                      80  
 Gly Lys Ser Ser Leu Leu Ser Ala Val Leu Gly Glu Leu Ala Pro Ser  
                                  85                      90                      95  
 His Gly Leu Val Ser Val His Gly Arg Ile Ala Tyr Val Ser Gln Gln  
                                  100                      105                      110  
 Pro Trp Val Phe Ser Gly Thr Leu Arg Ser Asn Ile Leu Phe Gly Lys  
                                  115                      120                      125  
 Lys Tyr Glu Lys Glu Arg Tyr Glu Lys Val Ile Lys Ala Cys Ala Leu  
                                  130                      135                      140  
 Lys Lys Asp Leu Gln Leu Leu Glu Asp Gly Asp Leu Thr Val Ile Gly  
                                  145                      150                      155                      160  
 Asp Arg Gly Thr Thr Leu Ser Gly Gly Gln Lys Ala Arg Val Asn Leu  
                                  165                      170                      175  
 Ala Arg Ala Val Tyr Gln Asp Ala Asp Ile Tyr Leu Leu Asp Asp Pro  
                                  180                      185                      190  
 Leu Ser Ala Val Asp Ala Glu Val Ser Arg His Leu Phe Glu Leu Cys  
                                  195                      200                      205  
 Ile Cys Gln Ile Leu His Glu Lys Ile Thr Ile Leu Val Thr His Gln  
                                  210                      215                      220  
 Leu Gln Tyr Leu Lys Ala Ala Ser Gln Ile Leu Ile Leu Lys Asp Gly  
                                  225                      230                      235                      240  
 Lys Met Val Gln Lys Gly Thr Tyr Thr Glu Phe Leu Lys Ser Gly Ile  
                                  245                      250                      255  
 Asp Phe Gly Ser Leu Leu Lys Lys Asp Asn Glu Glu Ser Glu Gln Pro  
                                  260                      265                      270  
 Pro Val Pro Gly Thr Pro Thr Leu Arg Asn Arg Thr Phe Ser Glu Ser  
                                  275                      280                      285  
 Ser Val Trp Ser Gln Gln Ser Ser Arg Pro Ser Leu Lys Asp Gly Ala  
                                  290                      295                      300  
 Leu Glu Ser Gln Asp Thr Glu Asn Val Pro Val Thr Leu Ser Glu Glu  
                                  305                      310                      315                      320  
 Asn Arg Ser Glu Gly Lys Val Gly Phe Gln Ala Tyr Lys Asn Tyr Phe

308

```

          325          330          335
Arg Ala Gly Ala His Trp Ile Val Phe Ile Phe Leu Ile Leu Glu His
          340          345          350
His His His His His
          355

```

<210> 827  
 <211> 96  
 <212> PRT  
 <213> Homo sapiens

```

<400> 827
Met Gly Ile Arg Glu Lys Phe Ala His Cys Thr Val Leu Thr Ile Ala
          5          10          15
His Arg Leu Asn Thr Ile Ile Asp Ser Asp Lys Ile Met Val Leu Asp
          20          25          30
Ser Gly Arg Leu Lys Glu Tyr Asp Glu Pro Tyr Val Leu Leu Gln Asn
          35          40          45
Lys Glu Ser Leu Phe Tyr Lys Met Val Gln Gln Leu Gly Lys Ala Glu
          50          55          60
Ala Ala Ala Leu Thr Glu Thr Ala Lys Gln Arg Trp Gly Phe Thr Met
          65          70          75          80
Leu Ala Arg Leu Val Ser Asn Ser Leu Glu His His His His His His
          85          90          95

```

<210> 828  
 <211> 35  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> PCR primer

```

<400> 828
cgcccatggg gatccgggag aaatttgccc actgc
                                     35

```

<210> 829  
 <211> 35  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> PCR primer

```

<400> 829
cgccctcgagg gagtttgaga ccagcctggc caaca
                                     35

```

<210> 830  
 <211> 38  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> PCR primer

<400> 830

309

gcatggacca tatgtcagcc attgagaggg tgtcagag

38

&lt;210&gt; 831

&lt;211&gt; 34

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; PCR primer

&lt;400&gt; 831

ccgctcgaga ataaggaaaa tgaagacaat ccag

34

&lt;210&gt; 832

&lt;211&gt; 27

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; PCR primer

&lt;400&gt; 832

gttgaattca tgcacggggc ccaggtg

27

&lt;210&gt; 833

&lt;211&gt; 30

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; PCR primer

&lt;400&gt; 833

cccctcgagt cactatggtc tgcctcttga

30

&lt;210&gt; 834

&lt;211&gt; 915

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 834

atgcatcacc atcaccatca cacggccgcg tccgataact tccagctgtc ccaggggtggg 60  
 cagggattcg ccattccgat cgggcaggcg atggcgatcg cgggccagat caagcttccc 120  
 accgttcata tcgggcctac cgccttcctc ggcttgggtg ttgtcgacaa caacggcaac 180  
 ggcgcacgag tccaacgcgt ggtcgggagc gctccggcgg caagtctcgg catctccacc 240  
 ggcgacgtga tcaccgcggt cgacggcgct ccgatcaact cggccaccgc gatggcggac 300  
 gcgcttaacg ggcatcatcc cgtgacgtc atctcgggtga cctggcaaac caagtcgggc 360  
 ggcacgcgta cagggaaacgt gacattggcc gagggacccc cggccgaatt catgcacggg 420  
 cccaggtgct tggcacgctg ctccgagtggt gcttgtcctg ccttggctgc cacctctgcg 480  
 ggggtgcgtc tggagggggg ggacgggcca ccaaccttac ccagtcaagg aagtggatgg 540  
 ccatgttccc acagcctgag tggctgccac ctgatggctg atggagcaaa ggccttagga 600  
 aaagcagatg gcccttgccc ctaccttttt gttagaagaa ctgatgttcc atgtcctgca 660  
 gcgagtgagg ttggtggctg tgcccgcagc tcctggcgcg ccctcgcaga ggtgactggg 720  
 tgctctttgg gccctcttgg ccttgcccag catgcacaag cctcagtgct actactgtgc 780

310

tacaaatgga gccatatagg ggaaacgagc agccatctca ggagcaaggt gtatgctgcc 840  
 ttggtgggct ccagtccttg cctcaagggt cttatgtcac tgtgggcttc ttggttgta 900  
 agaggcagac catag 915

&lt;210&gt; 835

&lt;211&gt; 304

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 835

Met His His His His His Thr Ala Ala Ser Asp Asn Phe Gln Leu  
                   5                  10                  15  
 Ser Gln Gly Gly Gln Gly Phe Ala Ile Pro Ile Gly Gln Ala Met Ala  
                   20                  25                  30  
 Ile Ala Gly Gln Ile Lys Leu Pro Thr Val His Ile Gly Pro Thr Ala  
                   35                  40                  45  
 Phe Leu Gly Leu Gly Val Val Asp Asn Asn Gly Asn Gly Ala Arg Val  
                   50                  55                  60  
 Gln Arg Val Val Gly Ser Ala Pro Ala Ala Ser Leu Gly Ile Ser Thr  
                   65                  70                  75                  80  
 Gly Asp Val Ile Thr Ala Val Asp Gly Ala Pro Ile Asn Ser Ala Thr  
                   85                  90                  95  
 Ala Met Ala Asp Ala Leu Asn Gly His His Pro Gly Asp Val Ile Ser  
                   100                  105                  110  
 Val Thr Trp Gln Thr Lys Ser Gly Gly Thr Arg Thr Gly Asn Val Thr  
                   115                  120                  125  
 Leu Ala Glu Gly Pro Pro Ala Glu Phe Met His Gly Pro Gln Val Leu  
                   130                  135                  140  
 Ala Arg Cys Ser Glu Cys Ala Cys Pro Ala Leu Ala Ala Thr Ser Ala  
                   145                  150                  155                  160  
 Gly Val Arg Leu Glu Gly Val Asp Arg Pro Pro Thr Leu Pro Ser Gln  
                   165                  170                  175  
 Gly Ser Gly Trp Pro Cys Ser His Ser Leu Ser Gly Cys His Leu Met  
                   180                  185                  190  
 Ala Asp Gly Ala Lys Ala Leu Gly Lys Ala Asp Gly Pro Trp Pro Tyr  
                   195                  200                  205  
 Leu Phe Val Arg Arg Thr Asp Val Pro Cys Pro Ala Ala Ser Glu Val  
                   210                  215                  220  
 Gly Gly Cys Ala Pro Ser Ser Trp Arg Ala Leu Ala Glu Val Thr Gly  
                   225                  230                  235                  240  
 Cys Ser Leu Gly Pro Leu Gly Leu Ala Gln His Ala Gln Ala Ser Val  
                   245                  250                  255  
 Leu Leu Leu Cys Tyr Lys Trp Ser His Ile Gly Glu Thr Ser Ser His  
                   260                  265                  270  
 Leu Arg Ser Lys Val Tyr Ala Ala Phe Gly Gly Ser Ser Pro Cys Leu  
                   275                  280                  285  
 Lys Gly Leu Met Ser Leu Trp Ala Ser Trp Leu Ser Arg Gly Arg Pro  
                   290                  295                  300

&lt;210&gt; 836

&lt;211&gt; 24

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; PCR primer

&lt;400&gt; 836

311

cgaagtcacg tggaggccag cctc

24

&lt;210&gt; 837

&lt;211&gt; 29

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; PCR primer

&lt;400&gt; 837

cctgaccgaa ttcattaact ggcttgac

29

&lt;210&gt; 838

&lt;211&gt; 166

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; VARIANT

&lt;222&gt; (1)...(166)

&lt;223&gt; Xaa = Any Amino Acid

&lt;400&gt; 838

Met	Gly	His	His	His	His	His	His	Val	Glu	Ala	Ser	Leu	Ser	Val	Arg
1				5					10				15		
His	Pro	Glu	Tyr	Asn	Arg	Pro	Leu	Leu	Ala	Asn	Asp	Leu	Met	Leu	Ile
			20					25				30			
Lys	Leu	Asp	Glu	Ser	Val	Ser	Glu	Ser	Asp	Thr	Ile	Arg	Ser	Ile	Ser
		35					40					45			
Ile	Ala	Ser	Gln	Cys	Pro	Thr	Ala	Gly	Asn	Ser	Cys	Leu	Val	Ser	Gly
	50					55					60				
Trp	Gly	Leu	Leu	Ala	Asn	Gly	Arg	Met	Pro	Thr	Val	Leu	Gln	Cys	Val
65					70					75				80	
Asn	Val	Ser	Val	Val	Ser	Glu	Glu	Val	Cys	Ser	Lys	Leu	Tyr	Asp	Pro
				85					90					95	
Leu	Tyr	His	Pro	Ser	Met	Phe	Cys	Ala	Gly	Gly	Gly	Gln	Xaa	Gln	Xaa
			100					105					110		
Asp	Ser	Cys	Asn	Gly	Asp	Ser	Gly	Gly	Pro	Leu	Ile	Cys	Asn	Gly	Tyr
		115					120					125			
Leu	Gln	Gly	Leu	Val	Ser	Phe	Gly	Lys	Ala	Pro	Cys	Gly	Gln	Val	Gly
	130					135					140				
Val	Pro	Gly	Val	Tyr	Thr	Asn	Leu	Cys	Lys	Phe	Thr	Glu	Trp	Ile	Glu
145					150					155					160
Lys	Thr	Val	Gln	Ala	Ser										
					165										

&lt;210&gt; 839

&lt;211&gt; 504

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(504)

&lt;223&gt; n = A,T,C or G



312

<400> 839  
 atgggccatc atcatcatca tcacgtggag gccagcctct ccgtacggca cccagagtac 60  
 aacagaccct tgctcgctaa cgacctcatg ctcaccaagt tggacgaatc cgtgtccgag 120  
 tctgacacca tccggagcat cagcattgct tcgcagtgcc ctaccgctgg gaactcttgc 180  
 ctcgtttctg gctgggggtct gctggcgaaac ggcagaatgc ctaccgtgct gcagtgcgtg 240  
 aacgtgtcgg tgggtgtctga ggaggtctgc agtaagctct atgaccgct gtaccacccc 300  
 agcatgttct gcgcggcgagg agggcaanac cagaangact cctgcaacgg tgactctggg 360  
 gggccccctga tctgcaacgg gtacttgcag ggccttgtgt ctttcggaaa agccccgtgt 420  
 ggccaagtgt gcgtgccagg tgtctacacc aacctctgca aattcactga gtggatagag 480  
 aaaaccgtcc aggccagtta atga 504

<210> 840  
 <211> 21  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> PCR primer

<400> 840  
 ctcagggttc cggagccgcg g 21

<210> 841  
 <211> 35  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> PCR primer

<400> 841  
 ctatagaatt cattacaaa aagctgggct ccagc 35

<210> 842  
 <211> 241  
 <212> PRT  
 <213> Homo sapiens

<400> 842  
 Met Gln His His His His His Leu Arg Val Pro Glu Pro Arg Pro  
 1 5 10 15  
 Gly Glu Ala Lys Ala Glu Gly Ala Ala Pro Pro Thr Pro Ser Lys Pro  
 20 25 30  
 Leu Thr Ser Phe Leu Ile Gln Asp Ile Leu Arg Asp Gly Ala Gln Arg  
 35 40 45  
 Gln Gly Gly Arg Thr Ser Ser Gln Arg Gln Arg Asp Pro Glu Pro Glu  
 50 55 60  
 Pro Glu Pro Glu Pro Glu Gly Gly Arg Ser Arg Ala Gly Ala Gln Asn  
 65 70 75 80  
 Asp Gln Leu Ser Thr Gly Pro Arg Ala Ala Pro Glu Glu Ala Glu Thr  
 85 90 95  
 Leu Ala Glu Thr Glu Pro Glu Arg His Leu Gly Ser Tyr Leu Leu Asp  
 100 105 110  
 Ser Glu Asn Thr Ser Gly Ala Leu Pro Arg Leu Pro Gln Thr Pro Lys  
 115 120 125

313

Gln Pro Gln Lys Arg Ser Arg Ala Ala Phe Ser His Thr Gln Val Ile  
 130 135 140  
 Glu Leu Glu Arg Lys Phe Ser His Gln Lys Tyr Leu Ser Ala Pro Glu  
 145 150 155 160  
 Arg Ala His Leu Ala Lys Asn Leu Lys Leu Thr Glu Thr Gln Val Lys  
 165 170 175  
 Ile Trp Phe Gln Asn Arg Arg Tyr Lys Thr Lys Arg Lys Gln Leu Ser  
 180 185 190  
 Ser Glu Leu Gly Asp Leu Glu Lys His Ser Ser Leu Pro Ala Leu Lys  
 195 200 205  
 Glu Glu Ala Phe Ser Arg Ala Ser Leu Val Ser Val Tyr Asn Ser Tyr  
 210 215 220  
 Pro Tyr Tyr Pro Tyr Leu Tyr Cys Val Gly Ser Trp Ser Pro Ala Phe  
 225 230 235 240  
 Trp

<210> 843  
 <211> 729  
 <212> DNA  
 <213> Homo sapiens

<400> 843  
 atgcagcatc accaccatca ccacctcagg gttccggagc cgcggcccg ggaggcgaaa 60  
 gcggaggggg ccgcgcccgc gaccccgctc aagccgctca cgtccttcct catccaggac 120  
 atcctgcccgg acggcgcgca gcggcaaggc ggccgcacga gcagccagag acagcgcgac 180  
 ccggagcccg agccagagcc agagccagag ggaggacgca gccgcgccc ggcgcgagaac 240  
 gaccagctga gcaccggggc ccgcgcccgc ccggatgagg ccgagacgct ggcagagacc 300  
 gagccagaaa ggcacttggg gtcttatctg ttggactctg aaaacacttc aggcgccctt 360  
 ccaaggcttc cccaaacccc taagcagccg cagaagcgct cccgagctgc cttctccac 420  
 actcaggtga tgcagttgga gaggaagttc agccatcaga agtacctgtc ggcccctgaa 480  
 cgggcccacc tggccaagaa cctcaagctc acggagaccc aagtgaagat atggttccag 540  
 aacagacgct ataagactaa gcgaaagcag ctctcctcgg agctgggaga cttggagaag 600  
 cactcctttt tgccggccct gaaagaggag gcctctccc gggcctccct ggtctccgtg 660  
 tataacagct atccttacta ccctacctg cactgcgtgg gcagctggag ccagctttt 720  
 tggtaatga 729

<210> 844  
 <211> 27  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> PCR primer

<400> 844  
 ctactaagcg ctggagtgg ggatcag

27

<210> 845  
 <211> 33  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> PCR primer

314

<400> 845  
catcgagaat tcactactct ctgactagat gtc

33

<210> 846  
<211> 161  
<212> PRT  
<213> Homo sapiens

<400> 846  
Met Gln His His His His His His Ala Gly Val Arg Asp Gln Gly Gln  
1 5 10 15  
Gly Ala Arg Trp Pro His Thr Gly Lys Arg Gly Pro Leu Leu Gln Gly  
20 25 30  
Leu Thr Trp Ala Thr Gly Gly His Cys Phe Ser Ser Glu Glu Ser Gly  
35 40 45  
Ala Val Asp Gly Ala Gly Gln Lys Lys Asp Arg Ala Trp Leu Arg Cys  
50 55 60  
Pro Glu Ala Val Ala Gly Phe Pro Leu Gly Ser Asp Cys Arg Glu Gly  
65 70 75 80  
Gly Arg Gln Gly Cys Gly Gly Ser Asp Asp Glu Asp Asp Leu Gly Val  
85 90 95  
Ala Pro Gly Leu Ala Pro Ala Trp Ala Leu Thr Gln Pro Pro Ser Gln  
100 105 110  
Ser Pro Gly Pro Gln Ser Leu Pro Ser Thr Pro Ser Ser Ile Trp Pro  
115 120 125  
Gln Trp Val Ile Leu Ile Thr Glu Leu Thr Ile Pro Ser Pro Ala His  
130 135 140  
Gly Pro Pro Trp Leu Pro Asn Ala Leu Glu Arg Gly His Leu Val Arg  
145 150 155 160  
Glu

<210> 847  
<211> 489  
<212> DNA  
<213> Homo sapiens

<400> 847  
atgcagcatc accaccatca ccacgctgga gtgagggatc aggggcaggg cgcgagatgg 60  
cctcacacag ggaagagagg gccctcctg cagggcctca cctgggccac aggaggacac 120  
tgcttttcct ctgaggagtc aggagctgtg gatggtgctg gacagaagaa ggacagggcc 180  
tggtcaggt gtccagaggc tgcgctggc ttccctttgg gatcagactg cagggaggga 240  
ggcggcaggg gttgtggggg gagtgcgat gaggatgacc tgggggtggc tccaggcctt 300  
gccctgcct gggccctcac ccagcctccc tcacagtctc ctggccctca gtctctcccc 360  
tccactccat cctccatctg gcctcagtg gtcattctga tcaactgaact gaccataccc 420  
agccctgccc acggccctcc atggtcctcc aatgccctgg agaggggaca tctagtcaga 480  
gagtagtga 489

<210> 848  
<211> 132  
<212> PRT  
<213> Homo sapiens

<400> 848  
Thr Ala Ala Ser Asp Asn Phe Gln Leu Ser Gln Gly Gly Gln Gly Phe

315

```

1           5           10           15
Ala Ile Pro Ile Gly Gln Ala Met Ala Ile Ala Gly Gln Ile Arg Ser
                20           25           30
Gly Gly Gly Ser Pro Thr Val His Ile Gly Pro Thr Ala Phe Leu Gly
                35           40           45
Leu Gly Val Val Asp Asn Asn Gly Asn Gly Ala Arg Val Gln Arg Val
                50           55           60
Val Gly Ser Ala Pro Ala Ala Ser Leu Gly Ile Ser Thr Gly Asp Val
                65           70           75           80
Ile Thr Ala Val Asp Gly Ala Pro Ile Asn Ser Ala Thr Ala Met Ala
                85           90           95
Asp Ala Leu Asn Gly His His Pro Gly Asp Val Ile Ser Val Asn Trp
                100          105          110
Gln Thr Lys Ser Gly Gly Thr Arg Thr Gly Asn Val Thr Leu Ala Glu
                115          120          125
Gly Pro Pro Ala
                130

```

<210> 849  
 <211> 31  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> PCR primer

<400> 849  
 gggaattca tcacctatgt gccgcctctg c 31

<210> 850  
 <211> 40  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> PCR primer

<400> 850  
 gggctcgagt cactcgccca cgaaatccgt gtaaacacgc 40

<210> 851  
 <211> 1203  
 <212> DNA  
 <213> Homo sapiens

<400> 851  
 atgcacatcacc atcaccatca cacggccgcg tccgataact tccagctgtc ccagggtggg 60  
 cagggattcg ccattccgat cgggcaggcg atggcgatcg cgggccagat caagcttccc 120  
 accgttcata tcgggcctac cgccttcctc ggcttgggtg ttgtcgacaa caacggcaac 180  
 ggcgcacgag tccaacgcgt ggtcgggagc gctccggcgg caagtctcgg catctccacc 240  
 ggcgacgtga tcaccgcggt cgacggcgct ccgatcaact cggccaccgc gatggcggac 300  
 gcgcttaacg ggcacatcc cggtgacgtc atctcgggtga cctggcaaac caagtcgggc 360  
 ggcacgcgta cagggaacgt gacattggcc gagggacccc cggccgaatt catcacctat 420  
 gtgcgcgctc tgctgctgga agtgggggta gaggagaagt tcatgaccat ggtgctgggc 480  
 attggtccaag tgctgggcct ggtctgtgtc ccgctcctag gctcagccag tgaccactgg 540  
 cgtggacgct atggccgcgc ccggcccttc atctgggcac tgtccttggg catcctgctg 600

316

```

agcctctttc tcatcccaag ggccggctgg ctagcagggc tgctgtgccc ggatcccagg 660
cccctggagc tggcactgct catcctgggc gtggggctgc tggacttctg tggccagggtg 720
tgcttcactc cactggaggc cctgctctct gacctcttcc gggaccgga ccactgtcgc 780
caggcctact ctgtctatgc cttcatgata agtcttgggg gctgcctggg ctacctcctg 840
cctgccattg actggyacac cagtgcctg gccccctacc tgggcaccca ggaggagtgc 900
ctctttggcc tgctcaccct catcttcctc acctgcgtag cagccacact gctggtggct 960
gaggaggcag cgctggggcc caccgagcca gcagaagggc tgtcggcccc ctcttgtcg 1020
ccccactgct gtccatgccg ggcccgttg gctttccgga acctgggcgc cctgcttccc 1080
cggctgcacc agctgtgctg ccgcatgccc cgcacctgc gccggctctt cgtgggtgag 1140
ctgtgcagct ggatggcact catgaccttc acgctgtttt acacggattt cgtgggcgag 1200
tga
1203

```

&lt;210&gt; 852

&lt;211&gt; 400

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 852

```

Met His His His His His His Thr Ala Ala Ser Asp Asn Phe Gln Leu
      5      10      15
Ser Gln Gly Gly Gln Gly Phe Ala Ile Pro Ile Gly Gln Ala Met Ala
      20      25      30
Ile Ala Gly Gln Ile Lys Leu Pro Thr Val His Ile Gly Pro Thr Ala
      35      40      45
Phe Leu Gly Leu Gly Val Val Asp Asn Asn Gly Asn Gly Ala Arg Val
      50      55      60
Gln Arg Val Val Gly Ser Ala Pro Ala Ala Ser Leu Gly Ile Ser Thr
      65      70      75      80
Gly Asp Val Ile Thr Ala Val Asp Gly Ala Pro Ile Asn Ser Ala Thr
      85      90      95
Ala Met Ala Asp Ala Leu Asn Gly His His Pro Gly Asp Val Ile Ser
      100     105     110
Val Thr Trp Gln Thr Lys Ser Gly Gly Thr Arg Thr Gly Asn Val Thr
      115     120     125
Leu Ala Glu Gly Pro Pro Ala Glu Phe Ile Thr Tyr Val Pro Pro Leu
      130     135     140
Leu Leu Glu Val Gly Val Glu Glu Lys Phe Met Thr Met Val Leu Gly
      145     150     155     160
Ile Gly Pro Val Leu Gly Leu Val Cys Val Pro Leu Leu Gly Ser Ala
      165     170     175
Ser Asp His Trp Arg Gly Arg Tyr Gly Arg Arg Arg Pro Phe Ile Trp
      180     185     190
Ala Leu Ser Leu Gly Ile Leu Leu Ser Leu Phe Leu Ile Pro Arg Ala
      195     200     205
Gly Trp Leu Ala Gly Leu Leu Cys Pro Asp Pro Arg Pro Leu Glu Leu
      210     215     220
Ala Leu Leu Ile Leu Gly Val Gly Leu Leu Asp Phe Cys Gly Gln Val
      225     230     235     240
Cys Phe Thr Pro Leu Glu Ala Leu Leu Ser Asp Leu Phe Arg Asp Pro
      245     250     255
Asp His Cys Arg Gln Ala Tyr Ser Val Tyr Ala Phe Met Ile Ser Leu
      260     265     270
Gly Gly Cys Leu Gly Tyr Leu Leu Pro Ala Ile Asp Trp Asp Thr Ser
      275     280     285
Ala Leu Ala Pro Tyr Leu Gly Thr Gln Glu Glu Cys Leu Phe Gly Leu
      290     295     300
Leu Thr Leu Ile Phe Leu Thr Cys Val Ala Ala Thr Leu Leu Val Ala
      305     310     315     320

```

317

Glu	Glu	Ala	Ala	Leu	Gly	Pro	Thr	Glu	Pro	Ala	Glu	Gly	Leu	Ser	Ala
				325	.				330					335	
Pro	Ser	Leu	Ser	Pro	His	Cys	Cys	Pro	Cys	Arg	Ala	Arg	Leu	Ala	Phe
				340				345					350		
Arg	Asn	Leu	Gly	Ala	Leu	Leu	Pro	Arg	Leu	His	Gln	Leu	Cys	Cys	Arg
		355					360					365			
Met	Pro	Arg	Thr	Leu	Arg	Arg	Leu	Phe	Val	Ala	Glu	Leu	Cys	Ser	Trp
		370				375					380				
Met	Ala	Leu	Met	Thr	Phe	Thr	Leu	Phe	Tyr	Thr	Asp	Phe	Val	Gly	Glu
385					390					395					400

```
<210> 853
<211> 20
<212> PRT
<213> Homo sapiens
```

```

<400> 853
Leu Leu Pro Pro Pro Pro Ala Leu Cys Gly Ala Ser Ala Cys Asp Val
                    5              10              15
Ser Val Arg Val
          20

```

```
<210> 854
<211> 60
<212> DNA
<213> Homo sapiens
```

<400> 854  
ctgctccac ctccaccgc gctctgctgg gcctctgct gtgatgtct cgtacgtgtg 60

```
<210> 855
<211> 10
<212> PRT
<213> Homo sapiens
```

```
<400> 855
Ala Ser Ala Cys Asp Val Ser Val Arg Val
          5                      10
```

```
<210> 856
<211> 30
<212> DNA
<213> Homo sapiens
```

<400> 856  
gcctctgcct gtgatgtctc cgtacgtgtg 30

```
<210> 857
<211> 9
<212> PRT
<213> Homo sapiens
```

<400> 857  
Ala Ser Ala Cys Asp Val Ser Val Arg  
1 5

<210> 858

318

<211> 9  
<212> PRT  
<213> Homo sapiens

<400> 858  
Ser Ala Cys Asp Val Ser Val Arg Val  
5

<210> 859  
<211> 27  
<212> DNA  
<213> Homo sapiens

<400> 859  
tctgcctgtg atgtctecgt acgtgtg

27

<210> 860  
<211> 19  
<212> PRT  
<213> Homo sapiens

<400> 860  
Gly Ile Gly Pro Val Leu Gly Leu Val Cys Val Pro Leu Leu Gly Ser  
5 10 15  
Ala Ser Asp

<210> 861  
<211> 19  
<212> PRT  
<213> Homo sapiens

<400> 861  
Val Pro Pro Leu Leu Leu Glu Val Gly Val Glu Glu Lys Phe Met Thr  
5 10 15  
Met Val Leu

<210> 862  
<211> 19  
<212> PRT  
<213> Homo sapiens

<400> 862  
Met Val Gln Arg Leu Trp Val Ser Arg Leu Leu Arg His Arg Lys Ala  
5 10 15  
Gln Leu Leu

<210> 863  
<211> 57  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(57)  
<223> n = A,T,C or G

<400> 863  
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<212> DNA  
<213> Homo sapiens

<220>  
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<223> n = A,T,C or G

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<212> DNA  
<213> Homo sapiens

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<210> 866  
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<212> PRT  
<213> Homo sapiens

<400> 866  
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1 5

<210> 867  
<211> 9  
<212> PRT  
<213> Homo sapiens

<400> 867  
Arg Met Pro Thr Val Leu Gln Cys Val  
1 5

<210> 868  
<211> 9  
<212> PRT  
<213> Homo sapiens

<400> 868  
Asn Leu Cys Lys Phe Thr Glu Trp Ile  
1 5



320

&lt;210&gt; 869

&lt;211&gt; 9

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 869

Met Leu Ile Lys Leu Asp Glu Ser Val

1 5

&lt;210&gt; 870

&lt;211&gt; 9

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 870

Leu Leu Ala Asn Asp Leu Met Leu Ile

1 5

&lt;210&gt; 871

&lt;211&gt; 10

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 871

Leu Leu Ala Asn Gly Arg Met Pro Thr Val

1 5 10

&lt;210&gt; 872

&lt;211&gt; 10

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 872

Leu Met Leu Ile Lys Leu Asp Glu Ser Val

1 5 10

&lt;210&gt; 873

&lt;211&gt; 10

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 873

Val Leu Gln Cys Val Asn Val Ser Val Val

1 5 10

&lt;210&gt; 874

&lt;211&gt; 10

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 874

Gly Leu Leu Ala Asn Gly Arg Met Pro Thr

1 5 10

&lt;210&gt; 875

&lt;211&gt; 10

&lt;212&gt; PRT

321

&lt;213&gt; Homo sapiens

&lt;400&gt; 875

Thr Val Leu Gln Cys Val Asn Val Ser Val  
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&lt;210&gt; 876

&lt;211&gt; 9

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 876

Gly Val Leu Val His Pro Gln Trp Val  
 1 5

&lt;210&gt; 877

&lt;211&gt; 9

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 877

Val Leu Val His Pro Gln Trp Val Leu  
 1 5

&lt;210&gt; 878

&lt;211&gt; 1195

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 878

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&lt;210&gt; 879

&lt;211&gt; 339

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

322

&lt;400&gt; 879

Met Glu Ser Arg Lys Asp Ile Thr Asn Gln Glu Glu Leu Trp Lys Met  
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 Lys Pro Arg Arg Asn Leu Glu Glu Asp Asp Tyr Leu His Lys Asp Thr  
                   20                  25                  30  
 Gly Glu Thr Ser Met Leu Lys Arg Pro Val Leu Leu His Leu His Gln  
                   35                  40                  45  
 Thr Ala His Ala Asp Glu Phe Asp Cys Pro Ser Glu Leu Gln His Thr  
                   50                  55                  60  
 Gln Glu Leu Phe Pro Gln Trp His Leu Pro Ile Lys Ile Ala Ala Ile  
                   65                  70                  75                  80  
 Ile Ala Ser Leu Thr Phe Leu Tyr Thr Leu Leu Arg Glu Val Ile His  
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 Pro Leu Ala Thr Ser His Gln Gln Tyr Phe Tyr Lys Ile Pro Ile Leu  
                   100                  105                  110  
 Val Ile Asn Lys Val Leu Pro Met Val Ser Ile Thr Leu Leu Ala Leu  
                   115                  120                  125  
 Val Tyr Leu Pro Gly Val Ile Ala Ala Ile Val Gln Leu His Asn Gly  
                   130                  135                  140  
 Thr Lys Tyr Lys Lys Phe Pro His Trp Leu Asp Lys Trp Met Leu Thr  
                   145                  150                  155                  160  
 Arg Lys Gln Phe Gly Leu Leu Ser Phe Phe Phe Ala Val Leu His Ala  
                   165                  170                  175  
 Ile Tyr Ser Leu Ser Tyr Pro Met Arg Arg Ser Tyr Arg Tyr Lys Leu  
                   180                  185                  190  
 Leu Asn Trp Ala Tyr Gln Gln Val Gln Gln Asn Lys Glu Asp Ala Trp  
                   195                  200                  205  
 Ile Glu His Asp Val Trp Arg Met Glu Ile Tyr Val Ser Leu Gly Ile  
                   210                  215                  220  
 Val Gly Leu Ala Ile Leu Ala Leu Leu Ala Val Thr Ser Ile Pro Ser  
                   225                  230                  235                  240  
 Val Ser Asp Ser Leu Thr Trp Arg Glu Phe His Tyr Ile Gln Ser Lys  
                   245                  250                  255  
 Leu Gly Ile Val Ser Leu Leu Leu Gly Thr Ile His Ala Leu Ile Phe  
                   260                  265                  270  
 Ala Trp Asn Lys Trp Ile Asp Ile Lys Gln Phe Val Trp Tyr Thr Pro  
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 Pro Thr Phe Met Ile Ala Val Phe Leu Pro Ile Val Val Leu Ile Phe  
                   290                  295                  300  
 Lys Ser Ile Leu Phe Leu Pro Cys Leu Arg Lys Lys Ile Leu Lys Ile  
                   305                  310                  315                  320  
 Arg His Gly Trp Glu Asp Val Thr Lys Ile Asn Lys Thr Glu Ile Cys  
                   325                  330                  335  
 Ser Gln Leu

&lt;210&gt; 880

&lt;211&gt; 2172

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 880

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2172

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&lt;210&gt; 881

&lt;211&gt; 2455

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 881

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324

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```

&lt;210&gt; 882

&lt;211&gt; 2455

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 882

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325

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&lt;210&gt; 883

&lt;211&gt; 62

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 883

```

Met Thr His Ser Ser Ala Trp Leu Glu Arg Pro Gln Glu Thr Tyr Asn
          5              10              15
His Gly Gly Arg Arg Gly Ser Lys Ala Arg Leu Thr Trp Trp Gln
          20              25              30
Glu Arg Thr Ser Glu Gly Gly Asp Cys His Lys Leu Phe Phe Phe Glu
          35              40              45
Thr Arg Val Trp Pro Cys Cys Pro Gly Trp Ser Ala Val Ala
          50              55              60

```

&lt;210&gt; 884

&lt;211&gt; 135

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 884

```

Met Val Glu Gly Glu Gly Glu Ala Arg His Val Leu His Gly Gly Arg
          5              10              15
Arg Glu Arg Val Arg Gly Glu Thr Ala Thr Asn Phe Phe Phe Leu Arg
          20              25              30
Gln Glu Ser Gly Pro Val Ala Gln Ala Gly Val Gln Trp His Asp Leu
          35              40              45
Ser Ser Leu Gln Pro Leu Pro His Arg Phe Lys Gln Phe Ser Cys Leu
          50              55              60
Ser Leu Pro His Ser Trp Asp His Arg Tyr Ala Pro Pro His Leu Ala
          65              70              75              80
Asn Phe Cys Ser Phe Ser Arg Asp Gly Val Ser Leu Cys Cys Ser Gly
          85              90              95
Trp Ser Lys Thr Pro Gly Leu Gln Gln Ser Ala Cys Leu Gly Leu Pro
          100             105             110
Lys Cys Trp Gly Tyr Arg His Lys Pro Pro His Pro Ala Cys His Ile
          115             120             125
Leu Leu Asn Tyr Gln Val Ser
          130             135

```

&lt;210&gt; 885

&lt;211&gt; 77

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 885

```

Met His Tyr His Lys Asn Ser Met Gly Lys Ile Pro Pro Ile Ile Gln

```

326

```

          5          10          15
Ser Pro Pro Thr Arg Ser Pro Pro Thr Arg Gly Ile Gly Trp Gly His
          20          25          30
Arg Ala Lys Pro Tyr Gln Met Leu Gln Gly Leu Gly Thr Leu Arg Pro
          35          40          45
Leu Arg Pro Gly Val Ser Val Thr Leu Leu Gly Ser Val Cys Leu Gln
          50          55          60
Asp Leu Pro Pro Leu Pro Trp Tyr Arg Arg Lys Val Leu
          65          70          75

```

&lt;210&gt; 886

&lt;211&gt; 60

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 886

```

Met Leu Val His Ile Tyr Ser Cys Cys Gly Met Val Tyr Arg Phe Gly
          5          10          15
Gln Met Ser Asp Asn Pro Phe Tyr Ile Leu Ala Ser Leu Gly Ser Ser
          20          25          30
Ser Cys Arg Asn Gly Leu Ala Ser Lys Trp Arg Gln Ala Asp Pro Ser
          35          40          45
Asp Gly Tyr Met Glu Pro Cys Phe Gln Leu Leu Phe
          50          55          60

```

&lt;210&gt; 887

&lt;211&gt; 76

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 887

```

Met Cys Leu Cys Ile Pro Leu Gly Gly Tyr Gln Glu Leu Cys His Cys
          5          10          15
Met Ser Thr Ser Asp Gly Phe Ala Pro Pro Gln Leu Gly Ser Arg
          20          25          30
Cys Ser His Ile Arg Gly Pro Ile Lys Ile Ala Arg Asn Lys Phe Pro
          35          40          45
Arg Thr Leu Thr Ser Gln Glu Leu Arg Arg Phe Ala Glu Tyr Ser Gly
          50          55          60
Met Met Phe Gly Asp Gln Thr Thr Ala Gly Gln Lys
          65          70          75

```

&lt;210&gt; 888

&lt;211&gt; 76

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 888

```

Met Val Lys Ser Arg Phe Thr Lys Asn Thr Lys Ile Thr Gln Ala Trp
          5          10          15
Trp Arg Ala Pro Val Ile Pro Gly Thr Arg Glu Ala Glu Gly Gly Glu
          20          25          30
Ser Leu Glu Pro Gly Arg Leu Arg Glu Glu Asn Arg Leu Asn Pro Gly
          35          40          45
Gly Arg Gly Cys Ser Glu Pro Arg Ser Cys Cys Cys Thr Pro Ala Trp
          50          55          60
Ser Thr Glu Gln Asp Ser Ala Ser Lys Thr Asn Lys
          65          70          75

```

327

&lt;210&gt; 889

&lt;211&gt; 80

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 889

```

Met Leu Leu His Ser Ser Leu Val Asn Arg Ala Arg Leu Cys Leu Lys
              5              10              15
Asn Lys Gln Ile Asn Lys Gln Thr Asn Lys Thr Glu Arg Phe Cys Cys
              20              25              30
Asn Val Gln Gly Ala Ile Cys Ser Phe Lys Lys Ile Ile Phe Gly Gln
              35              40              45
Ala Gln Trp Leu Thr Pro Val Ile Pro Ala Leu Trp Glu Ala Lys Val
              50              55              60
Gly Gly Ser Phe Glu Val Arg Ser Leu Arg Ser Ala Trp Pro Thr Trp
65              70              75              80

```

&lt;210&gt; 890

&lt;211&gt; 72

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 890

```

Met His Tyr His Lys Asn Ser Met Gly Lys Ile Pro Pro His Asn Pro
              5              10              15
Ile Thr Ser His Gln Val Ser Ser Asp Thr Trp Asp Trp Val Gly Thr
              20              25              30
Gln Ser Gln Thr Val Ser Asp Ala Ala Gly Ala Gly Asp Thr Glu Thr
              35              40              45
Thr Gln Thr Trp Cys Leu Cys His Ser Ser Gly Leu Cys Leu Ser Pro
              50              55              60
Gly Pro Pro Ser Pro Ser Met Val
65              70

```

&lt;210&gt; 891

&lt;211&gt; 77

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 891

```

Met His Tyr His Lys Asn Ser Met Gly Lys Ile Pro Pro Ile Ile Gln
              5              10              15
Ser Pro Pro Thr Arg Ser Pro Pro Thr Arg Gly Ile Gly Trp Gly His
              20              25              30
Arg Ala Lys Pro Tyr Gln Met Leu Gln Gly Leu Gly Thr Leu Arg Pro
              35              40              45
Leu Arg Pro Gly Val Ser Val Thr Leu Leu Gly Ser Val Cys Leu Gln
              50              55              60
Asp Leu Pro Pro Leu Pro Trp Tyr Arg Arg Lys Val Leu
65              70              75

```

&lt;210&gt; 892

&lt;211&gt; 60

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 892



328

```

Met Leu Val His Ile Tyr Ser Cys Cys Gly Met Val Tyr Arg Phe Gly
      5              10              15
Gln Met Ser Asp Asn Pro Phe Tyr Ile Leu Ala Ser Leu Gly Ser Ser
      20              25              30
Ser Cys Arg Asn Gly Leu Ala Ser Lys Trp Arg Gln Ala Asp Pro Ser
      35              40              45
Asp Gly Tyr Met Glu Pro Cys Phe Gln Leu Leu Phe
      50              55              60

```

&lt;210&gt; 893

&lt;211&gt; 76

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 893

```

Met Cys Leu Cys Ile Pro Leu Gly Gly Tyr Gln Glu Leu Cys His Cys
      5              10              15
Met Ser Thr Ser-Asp Gly Phe Ala Pro Pro Pro Gln Leu Gly Ser Arg
      20              25              30
Cys Ser His Ile Arg Gly Pro Ile Lys Ile Ala Arg Asn Lys Phe Pro
      35              40              45
Arg Thr Leu Thr Ser Gln Glu Leu Arg Arg Phe Ala Glu Tyr Ser Gly
      50              55              60
Met Met Phe Gly Asp Gln Thr Thr Ala Gly Gln Lys
      65              70              75

```

&lt;210&gt; 894

&lt;211&gt; 2479

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 894

```

gtcatattga acattccaga tacctatcat tactcgatgc tgttgataac agcaagatgg 60
ctttgaactc agggtcacca ccagctattg gaccttacta tgaaaacccat ggataccaac 120
cggaaaaccc ctatcccgca cagcccaactg tgggtccccc tggtctacgag gtgcatccgg 180
ctcagtacta cccgtccccc gtgccccagt acgccccgag ggtctcgacg caggcttcca 240
accccgctgt ctgcacgcag cccaaatccc catccgggac agtgtgcacc tcaaagacta 300
agaagcact gtgcatcacc ttgacctggt ggaccttccct cgtgggagct gcgctggccg 360
ctggcctact ctggaagttc atgggcagca agtgctccaa ctctgggata gagtgcgact 420
cctcagggtac ctgcatcaac ccctctaact ggtgtgatgg cgtgtcacac tgccccggcg 480
gggaggacga gaatcgggtgt gttcgctctt acggaccaa cttcatcctt cagatgtact 540
catctcagag gaagtcctgt caccctgtgt gccaaagcga ctggaacgag aactacgggc 600
gggcccctgt cagggacatg ggctataaga ataattttta ctctagccaa ggaatagtgg 660
atgacagcgg atccaccagc tttatgaaac tgaacacaag tgccggcaat gtcgatatct 720
ataaaaaact gtaccacagt gatgcctgtt cttcaaaagc agtggtttct ttacgctgtt 780
tagcctgcgg ggtcaacttg aactcaagcc gccagagcag gatcgtgggc ggtgagagcg 840
cgctcccggg ggccctggccc tggcagggtca gcctgcacgt ccagaacgtc cacgtgtgcg 900
gaggctccat catcaccccc gagtggatcg tgacagccgc ccactgcgtg gaaaaacctc 960
ttaacaatcc atggcatttg acggcatttg cggggatttt gagacaatct ttcatgttct 1020
atggagcccg ataccaagta caaaaagtga tttctcatcc aaattatgac tccaagacca 1080
agaacaatga cattgcgctg atgaagctgc agaagcctct gactttcaac gacctagtga 1140
aaccagtgtg tctgcccac ccaggcatga tgctgcagcc agaacagctc tgctggattt 1200
ccgggtgggg ggccaccgag gagaaaggga agacctcaga agtgctgaac gctgccaagg 1260
tgctttctcat tgagacacag agatgcaaca gcagatatgt ctatgacaac ctgatcacac 1320
cagccatgat ctgtgccggc ttctgcaggg ggaacgtcga ttcttgccag ggtgacagt 1380
gagggcctct ggtcacttcg aacaacaata tctggtggct gataggggat acaagctggg 1440
gttctgtctg tgccaaagct tacagaccag gagtgtacgg gaatgtgatg gtattcacgg 1500
actggattta tcgacaaatg aaggcaaacg gctaattccac atgggtcttcg tccttgacgt 1560

```

329

```

cgttttacaa gaaaacaatg gggctgggtt tgcttccccg tgcattgattt actcttagag 1620
atgattcaga ggtcacttca tttttattaa acagtgaact tgtctggctt tggcactctc 1680
tgccatactg tgcaggctgc agtggctccc ctgccagcc tgcctccctt aacccttgt 1740
ccgcaagggg tgatggccgg ctggttggg gcaactggcg tcaattgttg aaggaagagg 1800
gttgagggtt gccccattg agatcttcct gctgagtcct ttccaggggc caattttgga 1860
tgagcatgga gctgtcactt ctcagctgct ggatgacttg agatgaaaaa ggagagacat 1920
ggaaaggagg acagccaggt ggcacctgca gcggctgcc tctggggcca cttggtagt 1980
tccccagcct acttcacaag gggattttgc tgatgggttc ttagagcctt agcagccctg 2040
gatggtggcc agaaataaag ggaccagccc ttcatgggtg gtgacgtggt agtcacttgt 2100
aagggaagca gaaacatttt tgttcttatg gggtgagaat atagacagt cccttgggtg 2160
gaggaagca attgaaaagg aacttgccct gagcactcct ggtgcaggtc tccacctgca 2220
cattgggtgg ggctcctggg agggagactc agccttcttc ctcactctcc ctgacctgc 2280
tcctagcacc ctggagagt aatgcccctt ggtccctggc agggcgccaa gtttggcacc 2340
atgtcggcct cttcaggcct gatagtcatt ggaaattgag gtccatggg gaaatcaagg 2400
atgctcagtt taaggtagac tgtttccatg ttatgtttct acacattgat ggtggtgacc 2460
ctgagttcaa agccatctt
2479

```

&lt;210&gt; 895

&lt;211&gt; 492

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 895

```

Met Ala Leu Asn Ser Gly Ser Pro Pro Ala Ile Gly Pro Tyr Tyr Glu
      5      10      15
Asn His Gly Tyr Gln Pro Glu Asn Pro Tyr Pro Ala Gln Pro Thr Val
      20      25      30
Val Pro Thr Val Tyr Glu Val His Pro Ala Gln Tyr Tyr Pro Ser Pro
      35      40      45
Val Pro Gln Tyr Ala Pro Arg Val Leu Thr Gln Ala Ser Asn Pro Val
      50      55      60
Val Cys Thr Gln Pro Lys Ser Pro Ser Gly Thr Val Cys Thr Ser Lys
      65      70      75      80
Thr Lys Lys Ala Leu Cys Ile Thr Leu Thr Leu Gly Thr Phe Leu Val
      85      90      95
Gly Ala Ala Leu Ala Ala Gly Leu Leu Trp Lys Phe Met Gly Ser Lys
      100     105     110
Cys Ser Asn Ser Gly Ile Glu Cys Asp Ser Ser Gly Thr Cys Ile Asn
      115     120     125
Pro Ser Asn Trp Cys Asp Gly Val Ser His Cys Pro Gly Gly Glu Asp
      130     135     140
Glu Asn Arg Cys Val Arg Leu Tyr Gly Pro Asn Phe Ile Leu Gln Met
      145     150     155     160
Tyr Ser Ser Gln Arg Lys Ser Trp His Pro Val Cys Gln Asp Asp Trp
      165     170     175
Asn Glu Asn Tyr Gly Arg Ala Ala Cys Arg Asp Met Gly Tyr Lys Asn
      180     185     190
Asn Phe Tyr Ser Ser Gln Gly Ile Val Asp Asp Ser Gly Ser Thr Ser
      195     200     205
Phe Met Lys Leu Asn Thr Ser Ala Gly Asn Val Asp Ile Tyr Lys Lys
      210     215     220
Leu Tyr His Ser Asp Ala Cys Ser Ser Lys Ala Val Val Ser Leu Arg
      225     230     235     240
Cys Leu Ala Cys Gly Val Asn Leu Asn Ser Ser Arg Gln Ser Arg Ile
      245     250     255
Val Gly Gly Glu Ser Ala Leu Pro Gly Ala Trp Pro Trp Gln Val Ser
      260     265     270
Leu His Val Gln Asn Val His Val Cys Gly Gly Ser Ile Ile Thr Pro

```

			275					280				285				
Glu	Trp	Ile	Val	Thr	Ala	Ala	His	Cys	Val	Glu	Lys	Pro	Leu	Asn	Asn	
	290					295					300					
Pro	Trp	His	Trp	Thr	Ala	Phe	Ala	Gly	Ile	Leu	Arg	Gln	Ser	Phe	Met	
305					310					315					320	
Phe	Tyr	Gly	Ala	Gly	Tyr	Gln	Val	Gln	Lys	Val	Ile	Ser	His	Pro	Asn	
				325					330					335		
Tyr	Asp	Ser	Lys	Thr	Lys	Asn	Asn	Asp	Ile	Ala	Leu	Met	Lys	Leu	Gln	
			340					345					350			
Lys	Pro	Leu	Thr	Phe	Asn	Asp	Leu	Val	Lys	Pro	Val	Cys	Leu	Pro	Asn	
		355				360						365				
Pro	Gly	Met	Met	Leu	Gln	Pro	Glu	Gln	Leu	Cys	Trp	Ile	Ser	Gly	Trp	
	370					375					380					
Gly	Ala	Thr	Glu	Glu	Lys	Gly	Lys	Thr	Ser	Glu	Val	Leu	Asn	Ala	Ala	
385					390					395					400	
Lys	Val	Leu	Leu	Ile	Glu	Thr	Gln	Arg	Cys	Asn	Ser	Arg	Tyr	Val	Tyr	
				405					410					415		
Asp	Asn	Leu	Ile	Thr	Pro	Ala	Met	Ile	Cys	Ala	Gly	Phe	Leu	Gln	Gly	
			420					425				430				
Asn	Val	Asp	Ser	Cys	Gln	Gly	Asp	Ser	Gly	Gly	Pro	Leu	Val	Thr	Ser	
		435				440					445					
Asn	Asn	Asn	Ile	Trp	Trp	Leu	Ile	Gly	Asp	Thr	Ser	Trp	Gly	Ser	Gly	
	450					455					460					
Cys	Ala	Lys	Ala	Tyr	Arg	Pro	Gly	Val	Tyr	Gly	Asn	Val	Met	Val	Phe	
465				470					475						480	
Thr	Asp	Trp	Ile	Tyr	Arg	Gln	Met	Lys	Ala	Asn	Gly					
			485					490								

```
<210> 896
<211> 683
<212> DNA
<213> Homo sapiens
```

<400> 896							
gtcatattga	acattccaga	tacctatcat	tactcgatgc	tgttgataac	agcaagatgg		60
ctttgaactc	agggtcacca	caagctattg	gaccttata	tgaaaaccat	ggataccaac		120
cggaaaacc	ctatcccgca	cagcccactg	tgggtccccc	tgctctacag	gtgcctccg		180
ctcagtacta	cccgctcccc	gtgccccagt	agccccgag	ggtcctgacg	caggcttcca		240
accccgctcg	ctgcacgcag	cccaaattccc	catccgggac	agtgtgcacc	tcaaagacta		300
agaaagcact	gtgcataccc	ttgacctctg	ggaccttcct	cgtggggagc	gcgctggccg		360
ctggcctact	ctggaagttc	atgggcagca	agtgtctcca	ctctggggata	gagtgcgact		420
cctcaggtag	ctgcatacaac	ccctctaact	ggtgtgatgg	cgtgtcacac	tgccccggcg		480
gggaggacga	gaatcggtgt	gttcgcctct	acggacccaa	cttcctcctt	cagatgtact		540
catctcagag	gaagtcctg	caccctgtgt	gccaaagcga	ctggaacgag	aactacgggc		600
gggcggcctg	cagggcactg	ggctataaga	ataattttta	ctctagccaa	ggaatagtgg		660
atgacagcgg	atccaccagc						683

```
<210> 897
<211> 209
<212> PRT
<213> Homo sapiens
```

<400> 897  
Met Ala Leu Asn Ser Gly Ser Pro Pro Ala Ile Gly Pro Tyr Tyr Glu  
1 5 10 15

331

```

Asn His Gly Tyr Gln Pro Glu Asn Pro Tyr Pro Ala Gln Pro Thr Val
      20      25      30
Val Pro Thr Val Tyr Glu Val His Pro Ala Gln Tyr Tyr Pro Ser Pro
      35      40      45
Val Pro Gln Tyr Ala Pro Arg Val Leu Thr Gln Ala Ser Asn Pro Val
      50      55      60
Val Cys Thr Gln Pro Lys Ser Pro Ser Gly Thr Val Cys Thr Ser Lys
      65      70      75      80
Thr Lys Lys Ala Leu Cys Ile Thr Leu Thr Leu Gly Thr Phe Leu Val
      85      90      95
Gly Ala Ala Leu Ala Ala Gly Leu Leu Trp Lys Phe Met Gly Ser Lys
      100      105      110
Cys Ser Asn Ser Gly Ile Glu Cys Asp Ser Ser Gly Thr Cys Ile Asn
      115      120      125
Pro Ser Asn Trp Cys Asp Gly Val Ser His Cys Pro Gly Gly Glu Asp
      130      135      140
Glu Asn Arg Cys Val Arg Leu Tyr Gly Pro Asn Phe Ile Leu Gln Met
      145      150      155      160
Tyr Ser Ser Gln Arg Lys Ser Trp His Pro Val Cys Gln Asp Asp Trp
      165      170      175
Asn Glu Asn Tyr Gly Arg Ala Ala Cys Arg Asp Met Gly Tyr Lys Asn
      180      185      190
Asn Phe Tyr Ser Ser Gln Gly Ile Val Asp Asp Ser Gly Ser Thr Ser
      195      200      205
Phe

```

```

<210> 898
<211> 27
<212> PRT
<213> Homo sapiens

```

```

<400> 898
Val Gly Glu Gly Leu Tyr Gln Gly Val Pro Arg Ala Glu Pro Gly Thr
  1           5           10           15
Glu Ala Arg Arg His Tyr Asp Glu Gly Val Arg
      20      25

```

```

<210> 899
<211> 35
<212> DNA
<213> Artificial Sequence

```

```

<220>
<223> PCR primer

```

```

<400> 899
ggatccgccg ccaccatgtc actttctagc ctgct

```

35

```

<210> 900
<211> 27
<212> DNA
<213> Artificial Sequence

```

```

<220>
<223> PCR primer

```

```

<400> 900

```

332

gtcgactcag ctggaccaca gccgcag

27

&lt;210&gt; 901

&lt;211&gt; 34

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; PCR primer

&lt;400&gt; 901

ggatccgccg ccacatggg ctgcaggctg ctct

34

&lt;210&gt; 902

&lt;211&gt; 27

&lt;212&gt; DNA

&lt;213&gt; Artificial Sequence

&lt;220&gt;

&lt;223&gt; PCR primer

&lt;400&gt; 902

gtcgactcag aaatcctttc tcttgac

27

&lt;210&gt; 903

&lt;211&gt; 936

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...()

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 903

```

atgggctgca ggctgntctg ctgtgcggtt ctctgtctcc tgggagcggg ccccatggaa 60
acgggagtta cgcagacacc aagacacctg gtcattggaa tgacaaataa gaagtctttg 120
aaatgtgaac aacatctggg tcataacgct atgtattggt acaagcaaag tgctaagaag 180
ccactggagc tcatgtttgt ctacagtctt gaagaacggg ttgaaaacaa cagtgtgcca 240
agtcgcttct cacctgaatg ccccaacagc tctcacttat tccttcacct acacaccctg 300
cagccagaag actcggccct gtatctctgc gccagcagcc aagaccggac aagcagctcc 360
tacgagcagt acttcgggccc gggcaccagg ctcacgggtc cagaggacct gaaaaacgtg 420
ttcccaccgg aggtcgctgt gtttgagcca tcagaagcag agatctocca caccctaaaag 480
gccacactgg tgtgcctggc cacaggcttc taccocgacc acgtggagct gagctggtgg 540
gtgaatggga aggagggtgca cagtggggtc agcacagacc cgcagcccct caaggagcag 600
cccgcctca atgactccag atactgcctg agcagccgcc tgagggtctc ggccaccttc 660
tggcagaacc cccgcaacca cttcogctgt caagtccagt tctacgggct ctcggagaat 720
gacgagtgga cccaggatag ggccaaacct gtcacccaga tcgtcagcgc cgaggcctgg 780
ggtagagcag actgtggctt cacctccgag tcttaccagc aaggggtcct gtctgccacc 840
atcctctatg agatcttgct agggaaggcc accttgatg ccgtgctggt cagtgccttc 900
gtgctgatgg ccatggtcaa gagaaaggat ttctga 936

```

&lt;210&gt; 904

&lt;211&gt; 834

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

333

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...()

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 904

```

atgtcacttt ctagcctgct naagggtggtc acagcttcac tgtggctagg acctggcatt 60
gccagaaga taactcaaac ccaaccagga atgttcgtgc agggaaaagga ggctgtgact 120
ctggactgca catatgacac cagtgatcaa agttatggtc tcttctggta caagcagccc 180
agcagtgggg aaatgatttt tcttatttat caggggtcct atgacgagca aaatgcaaca 240
gaaggtcgct actcattgaa tttccagaag gcaagaaaat ccgccaacct tgtcatctcc 300
gtttcacaac tgggggactc agcaatgtat ttctgtgcaa tgagagaggg cgcgggagga 360
ggaacaaaac tcacctttgg gacaggcact cagctaaaag tggaactcaa tatccagaac 420
cctgaccctg ccgtgtacca gctgagagac tctaaatcca gtgacaagtc tgtctgccta 480
ttcaccgatt ttgattctca aacaaatgtg tcacaaagta aggattctga tgtgtatatc 540
acagacaaaa ctgtgctaga catgaggtct atggacttca agagcaacag tgctgtggcc 600
tggagcaaca aatctgactt tgcatgtgca aacgccttca acaacagcat tattccagaa 660
gacaccttct tcccagccc agaaagttcc tgtgatgtca agctgggtcga gaaaagcttt 720
gaaacagata cgaacctaaa ctttcaaaac ctgtcagtga ttgggttccg aatcctcctc 780
ctgaaagtgg ccgggtttta tctgctcatg acgctgcggc tgtggtccag ctga      834

```

&lt;210&gt; 905

&lt;211&gt; 311

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; variant

&lt;222&gt; (1)...(311)

&lt;223&gt; Xaa = Any amino acid

&lt;400&gt; 905

```

Met Gly Cys Arg Leu Xaa Cys Cys Ala Val Leu Cys Leu Leu Gly Ala
      5              10              15
Val Pro Met Glu Thr Gly Val Thr Gln Thr Pro Arg His Leu Val Met
      20              25              30
Gly Met Thr Asn Lys Lys Ser Leu Lys Cys Glu Gln His Leu Gly His
      35              40              45
Asn Ala Met Tyr Trp Tyr Lys Gln Ser Ala Lys Lys Pro Leu Glu Leu
      50              55              60
Met Phe Val Tyr Ser Leu Glu Glu Arg Val Glu Asn Asn Ser Val Pro
      65              70              75              80
Ser Arg Phe Ser Pro Glu Cys Pro Asn Ser Ser His Leu Phe Leu His
      85              90              95
Leu His Thr Leu Gln Pro Glu Asp Ser Ala Leu Tyr Leu Cys Ala Ser
      100             105             110
Ser Gln Asp Arg Thr Ser Ser Ser Tyr Glu Gln Tyr Phe Gly Pro Gly
      115             120             125
Thr Arg Leu Thr Val Thr Glu Asp Leu Lys Asn Val Phe Pro Pro Glu
      130             135             140
Val Ala Val Phe Glu Pro Ser Glu Ala Glu Ile Ser His Thr Gln Lys
      145             150             155             160
Ala Thr Leu Val Cys Leu Ala Thr Gly Phe Tyr Pro Asp His Val Glu
      165             170             175
Leu Ser Trp Trp Val Asn Gly Lys Glu Val His Ser Gly Val Ser Thr
      180             185             190
Asp Pro Gln Pro Leu Lys Glu Gln Pro Ala Leu Asn Asp Ser Arg Tyr
      195             200             205

```

334

Cys Leu Ser Ser Arg Leu Arg Val Ser Ala Thr Phe Trp Gln Asn Pro  
 210 215 220  
 Arg Asn His Phe Arg Cys Gln Val Gln Phe Tyr Gly Leu Ser Glu Asn  
 225 230 235 240  
 Asp Glu Trp Thr Gln Asp Arg Ala Lys Pro Val Thr Gln Ile Val Ser  
 245 250 255  
 Ala Glu Ala Trp Gly Arg Ala Asp Cys Gly Phe Thr Ser Glu Ser Tyr  
 260 265 270  
 Gln Gln Gly Val Leu Ser Ala Thr Ile Leu Tyr Glu Ile Leu Leu Gly  
 275 280 285  
 Lys Ala Thr Leu Tyr Ala Val Leu Val Ser Ala Leu Val Leu Met Ala  
 290 295 300  
 Met Val Lys Arg Lys Asp Phe  
 305 310

<210> 906  
 <211> 277  
 <212> PRT  
 <213> Homo sapiens

<400> 906  
 Met Ser Leu Ser Ser Leu Leu Lys Val Val Thr Ala Ser Leu Trp Leu  
 5 10 15  
 Gly Pro Gly Ile Ala Gln Lys Ile Thr Gln Thr Gln Pro Gly Met Phe  
 20 25 30  
 Val Gln Glu Lys Glu Ala Val Thr Leu Asp Cys Thr Tyr Asp Thr Ser  
 35 40 45  
 Asp Gln Ser Tyr Gly Leu Phe Trp Tyr Lys Gln Pro Ser Ser Gly Glu  
 50 55 60  
 Met Ile Phe Leu Ile Tyr Gln Gly Ser Tyr Asp Glu Gln Asn Ala Thr  
 65 70 75 80  
 Glu Gly Arg Tyr Ser Leu Asn Phe Gln Lys Ala Arg Lys Ser Ala Asn  
 85 90 95  
 Leu Val Ile Ser Ala Ser Gln Leu Gly Asp Ser Ala Met Tyr Phe Cys  
 100 105 110  
 Ala Met Arg Glu Gly Ala Gly Gly Gly Asn Lys Leu Thr Phe Gly Thr  
 115 120 125  
 Gly Thr Gln Leu Lys Val Glu Leu Asn Ile Gln Asn Pro Asp Pro Ala  
 130 135 140  
 Val Tyr Gln Leu Arg Asp Ser Lys Ser Ser Asp Lys Ser Val Cys Leu  
 145 150 155 160  
 Phe Thr Asp Phe Asp Ser Gln Thr Asn Val Ser Gln Ser Lys Asp Ser  
 165 170 175  
 Asp Val Tyr Ile Thr Asp Lys Thr Val Leu Asp Met Arg Ser Met Asp  
 180 185 190  
 Phe Lys Ser Asn Ser Ala Val Ala Trp Ser Asn Lys Ser Asp Phe Ala  
 195 200 205  
 Cys Ala Asn Ala Phe Asn Asn Ser Ile Ile Pro Glu Asp Thr Phe Phe  
 210 215 220  
 Pro Ser Pro Glu Ser Ser Cys Asp Val Lys Leu Val Glu Lys Ser Phe  
 225 230 235 240  
 Glu Thr Asp Thr Asn Leu Asn Phe Gln Asn Leu Ser Val Ile Gly Phe  
 245 250 255  
 Arg Ile Leu Leu Leu Lys Val Ala Gly Phe Asn Leu Leu Met Thr Leu  
 260 265 270  
 Arg Leu Trp Ser Ser  
 275

335

<210> 907  
<211> 1536  
<212> DNA  
<213> Homo sapiens

<400> 907  
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gagctggtga gcctcaagtga gaagcggtag gggcgccgt acttctgcat gctgggtgcc 360  
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gaagcctaca tgaccctaa ggacgatata cggctggctg gggagctggt gactgtcatt 540  
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<210> 908  
<211> 1533  
<212> DNA  
<213> Homo sapiens

<400> 908  
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atgtttcagc acctgatgca gaagcggaag cacaccaggt ggacgtatgg accactgacc 180  
tcgactctct atgacctcac agagatcgac tcctcagggg atgagcagtc cctgctggaa 240  
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336

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ctggaggacg gggagagctg ggaatatcag atc 1533

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&lt;210&gt; 909

&lt;211&gt; 511

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 909

```

Met Tyr Asn Leu Leu Leu Ser Tyr Asp Arg His Gly Asp His Leu Gln
      5              10              15
Pro Leu Asp Leu Val Pro Asn His Gln Gly Leu Thr Pro Phe Lys Leu
      20              25              30
Ala Gly Val Glu Gly Asn Thr Val Met Phe Gln His Leu Met Gln Lys
      35              40              45
Arg Lys His Thr Gln Trp Thr Tyr Gly Pro Leu Thr Ser Thr Leu Tyr
      50              55              60
Asp Leu Thr Glu Ile Asp Ser Ser Gly Asp Glu Gln Ser Leu Leu Glu
      65              70              75
Leu Ile Ile Thr Thr Lys Lys Arg Glu Ala Arg Gln Ile Leu Asp Gln
      85              90              95
Thr Pro Val Lys Glu Leu Val Ser Leu Lys Trp Lys Arg Tyr Gly Arg
      100             105             110
Pro Tyr Phe Cys Met Leu Gly Ala Ile Tyr Leu Leu Tyr Ile Ile Cys
      115             120             125
Phe Thr Met Cys Cys Ile Tyr Arg Pro Leu Lys Pro Arg Thr Asn Asn
      130             135             140
Arg Thr Ser Pro Arg Asp Asn Thr Leu Leu Gln Gln Lys Leu Leu Gln
      145             150             155
Glu Ala Tyr Met Thr Pro Lys Asp Asp Ile Arg Leu Val Gly Glu Leu
      165             170             175
Val Thr Val Ile Gly Ala Ile Ile Ile Leu Leu Val Glu Val Pro Asp
      180             185             190
Ile Phe Arg Met Gly Val Thr Arg Phe Phe Gly Gln Thr Ile Leu Gly
      195             200             205
Gly Pro Phe His Val Leu Ile Ile Thr Tyr Ala Phe Met Val Leu Val
      210             215             220
Thr Met Val Met Arg Leu Ile Ser Ala Ser Gly Glu Val Val Pro Met
      225             230             235
Ser Phe Ala Leu Val Leu Gly Trp Cys Asn Val Met Tyr Phe Ala Arg
      245             250             255
Gly Phe Gln Met Leu Gly Pro Phe Thr Ile Met Ile Gln Lys Met Ile
      260             265             270
Phe Gly Asp Leu Met Arg Phe Cys Trp Leu Met Ala Val Val Ile Leu
      275             280             285
Gly Phe Ala Ser Ala Phe Tyr Ile Ile Phe Gln Thr Glu Asp Pro Glu
      290             295             300
Glu Leu Gly His Phe Tyr Asp Tyr Pro Met Ala Leu Phe Ser Thr Phe
      305             310             315
Glu Leu Phe Leu Thr Ile Ile Asp Gly Pro Ala Asn Tyr Asn Val Asp
      325             330             335
Leu Pro Phe Met Tyr Ser Ile Thr Tyr Ala Ala Phe Ala Ile Ile Ala

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337

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      340      345      350
Thr Leu Leu Met Leu Asn Leu Leu Ile Ala Met Met Gly Asp Thr His
      355      360      365
Trp Arg Val Ala His Glu Arg Asp Glu Leu Trp Arg Ala Gln Ile Val
      370      375      380
Ala Thr Thr Val Met Leu Glu Arg Lys Leu Pro Arg Cys Leu Trp Pro
385      390      395      400
Arg Ser Gly Ile Cys Gly Arg Glu Tyr Gly Leu Gly Asp Arg Trp Phe
      405      410      415
Leu Arg Val Glu Asp Arg Gln Asp Leu Asn Arg Gln Arg Ile Gln Arg
      420      425      430
Tyr Ala Gln Ala Phe His Thr Arg Gly Ser Glu Asp Leu Asp Lys Asp
      435      440      445
Ser Val Glu Lys Leu Glu Leu Gly Cys Pro Phe Ser Pro His Leu Ser
450      455      460
Leu Pro Met Pro Ser Val Ser Arg Ser Thr Ser Arg Ser Ser Ala Asn
465      470      475      480
Trp Glu Arg Leu Arg Gln Gly Thr Leu Arg Arg Asp Leu Arg Gly Ile
      485      490      495
Ile Asn Arg Gly Leu Glu Asp Gly Glu Ser Trp Glu Tyr Gln Ile
      500      505      510

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&lt;210&gt; 910

&lt;211&gt; 134

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 910

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Met Tyr Asn Leu Leu Ser Tyr Asp Arg His Gly Asp His Leu Gln
      5      10      15
Pro Leu Asp Leu Val Pro Asn His Gln Gly Leu Thr Pro Phe Lys Leu
      20      25      30
Ala Gly Val Glu Gly Asn Thr Val Met Phe Gln His Leu Met Gln Lys
      35      40      45
Arg Lys His Thr Gln Trp Thr Tyr Gly Pro Leu Thr Ser Thr Leu Tyr
      50      55      60
Asp Leu Thr Glu Ile Asp Ser Ser Gly Asp Glu Gln Ser Leu Leu Glu
      65      70      75      80
Leu Ile Ile Thr Thr Lys Lys Arg Glu Ala Arg Gln Ile Leu Asp Gln
      85      90      95
Thr Pro Val Lys Glu Leu Val Ser Leu Lys Trp Lys Arg Tyr Gly Arg
      100      105      110
Pro Tyr Phe Cys Met Leu Gly Ala Ile Tyr Leu Leu Tyr Ile Ile Cys
      115      120      125
Phe Thr Met Cys Cys Ile
      130

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&lt;210&gt; 911

&lt;211&gt; 55

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 911

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Ala Tyr Arg Pro Leu Lys Pro Arg Thr Asn Asn Arg Thr Ser Pro Arg
      5      10      15
Asp Asn Thr Leu Leu Gln Gln Lys Leu Leu Gln Glu Ala Tyr Met Thr
      20      25      30
Pro Lys Asp Asp Ile Arg Leu Val Gly Glu Leu Val Thr Val Ile Gly

```

338

35 40 45  
 Ala Ile Ile Ile Leu Leu Val  
 50 55

<210> 912  
 <211> 39  
 <212> PRT  
 <213> Homo sapiens

<400> 912  
 Glu Val Pro Asp Ile Phe Arg Met Gly Val Thr Arg Phe Phe Gly Gln  
 5 10 15  
 Thr Ile Leu Gly Gly Pro Phe His Val Leu Ile Ile Thr Tyr Ala Phe  
 20 25 30  
 Met Val Leu Val Thr Met Val  
 35

<210> 913  
 <211> 19  
 <212> PRT  
 <213> Homo sapiens

<400> 913  
 Met Arg Leu Ile Ser Ala Ser Gly Glu Val Val Pro Met Ser Phe Ala  
 5 10 15  
 Leu Val Leu

<210> 914  
 <211> 52  
 <212> PRT  
 <213> Homo sapiens

<400> 914  
 Gly Trp Cys Asn Val Met Tyr Phe Ala Arg Gly Phe Gln Met Leu Gly  
 5 10 15  
 Pro Phe Thr Ile Met Ile Gln Lys Met Ile Phe Gly Asp Leu Met Arg  
 20 25 30  
 Phe Cys Trp Leu Met Ala Val Val Ile Leu Gly Phe Ala Ser Ala Phe  
 35 40 45  
 Tyr Ile Ile Phe  
 50

<210> 915  
 <211> 213  
 <212> PRT  
 <213> Homo sapiens

<400> 915  
 Gln Thr Glu Asp Pro Glu Glu Leu Gly His Phe Tyr Asp Tyr Pro Met  
 5 10 15  
 Ala Leu Phe Ser Thr Phe Glu Leu Phe Leu Thr Ile Ile Asp Gly Pro  
 20 25 30  
 Ala Asn Tyr Asn Val Asp Leu Pro Phe Met Tyr Ser Ile Thr Tyr Ala  
 35 40 45  
 Ala Phe Ala Ile Ile Ala Thr Leu Leu Met Leu Asn Leu Leu Ile Ala  
 50 55 60  
 Met Met Gly Asp Thr His Trp Arg Val Ala His Glu Arg Asp Glu Leu

339

65					70					75				80	
Trp	Arg	Ala	Gln	Ile	Val	Ala	Thr	Thr	Val	Met	Leu	Glu	Arg	Lys	Leu
				85					90					95	
Pro	Arg	Cys	Leu	Trp	Pro	Arg	Ser	Gly	Ile	Cys	Gly	Arg	Glu	Tyr	Gly
			100					105					110		
Leu	Gly	Asp	Arg	Trp	Phe	Leu	Arg	Val	Glu	Asp	Arg	Gln	Asp	Leu	Asn
		115					120					125			
Arg	Gln	Arg	Ile	Gln	Arg	Tyr	Ala	Gln	Ala	Phe	His	Thr	Arg	Gly	Ser
		130				135					140				
Glu	Asp	Leu	Asp	Lys	Asp	Ser	Val	Glu	Lys	Leu	Glu	Leu	Gly	Cys	Pro
		145			150					155					160
Phe	Ser	Pro	His	Leu	Ser	Leu	Pro	Met	Pro	Ser	Val	Ser	Arg	Ser	Thr
			165					170						175	
Ser	Arg	Ser	Ser	Ala	Asn	Trp	Glu	Arg	Leu	Arg	Gln	Gly	Thr	Leu	Arg
			180					185					190		
Arg	Asp	Leu	Arg	Gly	Ile	Ile	Asn	Arg	Gly	Leu	Glu	Asp	Gly	Glu	Ser
		195					200					205			
Trp	Glu	Tyr	Gln	Ile											
			210												

&lt;210&gt; 916

&lt;211&gt; 1302

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 916

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ttcatcctaa taggcctccc tggtttagaa gaggctcagt tctggttggc cttcccattg 180
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gagcacagcc tgcattgagcc catgtatata tttctttgca tgctttcagg cattgacatc 300
ctcatctcca cctcatccat gcccaaatg ctggccatct tctggttcaa ttccactacc 360
atccagtttg atgcttgtct gctacagatg tttgccatcc actccttacc tggcatggaa 420
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&lt;210&gt; 917

&lt;211&gt; 2061

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 917

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acgattcgac agcgcattcct tcgacttttc catgtggcca cacacgcttc agagccctag 60
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340

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2061

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&lt;210&gt; 918

&lt;211&gt; 957

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 918

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attcgacagc gcatccttcg acttttccat gtggccacac acgcttcaga gccctag 957

```

&lt;210&gt; 919

341

<211> 954  
 <212> DNA  
 <213> Homo sapiens

<400> 919  
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<210> 920  
 <211> 318  
 <212> PRT  
 <213> Homo sapiens

<400> 920  
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                   5                  10                  15  
 Leu Ile Gly Leu Pro Gly Leu Glu Glu Ala Gln Phe Trp Leu Ala Phe  
                   20                  25                  30  
 Pro Leu Cys Ser Leu Tyr Leu Ile Ala Val Leu Gly Asn Leu Thr Ile  
                   35                  40                  45  
 Ile Tyr Ile Val Arg Thr Glu His Ser Leu His Glu Pro Met Tyr Ile  
                   50                  55                  60  
 Phe Leu Cys Met Leu Ser Gly Ile Asp Ile Leu Ile Ser Thr Ser Ser  
                   65                  70                  75                  80  
 Met Pro Lys Met Leu Ala Ile Phe Trp Phe Asn Ser Thr Thr Ile Gln  
                   85                  90                  95  
 Phe Asp Ala Cys Leu Leu Gln Met Phe Ala Ile His Ser Leu Ser Gly  
                   100                  105                  110  
 Met Glu Ser Thr Val Leu Leu Ala Met Ala Phe Asp Arg Tyr Val Ala  
                   115                  120                  125  
 Ile Cys His Pro Leu Arg His Ala Thr Val Leu Thr Leu Pro Arg Val  
                   130                  135                  140  
 Thr Lys Ile Gly Val Ala Ala Val Val Arg Gly Ala Ala Leu Met Ala  
                   145                  150                  155                  160  
 Pro Leu Pro Val Phe Ile Lys Gln Leu Pro Phe Cys Arg Ser Asn Ile  
                   165                  170                  175  
 Leu Ser His Ser Tyr Cys Leu His Gln Asp Val Met Lys Leu Ala Cys  
                   180                  185                  190  
 Asp Asp Ile Arg Val Asn Val Val Tyr Gly Leu Ile Val Ile Ile Ser  
                   195                  200                  205  
 Ala Ile Gly Leu Asp Ser Leu Leu Ile Ser Phe Ser Tyr Leu Leu Ile  
                   210                  215                  220  
 Leu Lys Thr Val Leu Gly Leu Thr Arg Glu Ala Gln Ala Lys Ala Phe  
                   225                  230                  235                  240

342

Gly Thr Cys Val Ser His Val Cys Ala Val Phe Ile Phe Tyr Val Pro  
                   245                  250                  255  
 Phe Ile Gly Leu Ser Met Val His Arg Phe Ser Lys Arg Arg Asp Ser  
                   260                  265                  270  
 Pro Leu Pro Val Ile Leu Ala Asn Ile Tyr Leu Leu Val Pro Pro Val  
                   275                  280                  285  
 Leu Asn Pro Ile Val Tyr Gly Val Lys Thr Lys Glu Ile Arg Gln Arg  
                   290                  295                  300  
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 <212> PRT  
 <213> Homo sapiens

<400> 921  
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<210> 923  
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 <212> PRT  
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<400> 923  
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 Ala Cys Leu Leu Gln  
                   20

<210> 924  
 <211> 20  
 <212> PRT  
 <213> Homo sapiens

<400> 924  
 Asp Arg Tyr Val Ala Ile Cys His Pro Leu Arg His Ala Thr Val Leu  
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 Thr Leu Pro Arg  
                   20

<210> 925  
 <211> 37  
 <212> PRT  
 <213> Homo sapiens

343

&lt;400&gt; 925

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Phe Ile Lys Gln Leu Pro Phe Cys Arg Ser Asn Ile Leu Ser His Ser
      5              10              15
Tyr Cys Leu His Gln Asp Val Met Lys Leu Ala Cys Asp Asp Ile Arg
      20              25              30
Val Asn Val Val Tyr
      35

```

&lt;210&gt; 926

&lt;211&gt; 13

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 926

```

Lys Thr Val Leu Gly Leu Thr Arg Glu Ala Gln Ala Lys
      5              10

```

&lt;210&gt; 927

&lt;211&gt; 10

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 927

```

Val His Arg Phe Ser Lys Arg Arg Asp Ser
      5              10

```

&lt;210&gt; 928

&lt;211&gt; 22

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 928

```

Lys Thr Lys Glu Ile Arg Gln Arg Ile Leu Arg Leu Phe His Val Ala
      5              10              15

```

```

Thr His Ala Ser Glu Pro
      20

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&lt;210&gt; 929

&lt;211&gt; 3245

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 929

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gccgc
3245

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&lt;210&gt; 930

&lt;211&gt; 1479

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 930

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345

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<210> 931  
 <211> 1476  
 <212> DNA  
 <213> Homo sapiens

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<400> 931
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<210> 932  
 <211> 492  
 <212> PRT  
 <213> Homo sapiens

<400> 932

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Val	Pro	Thr	Val	Tyr	Glu	Val	His	Pro	Ala	Gln	Tyr	Tyr	Pro	Ser	Pro
Val	Pro	Gln	Tyr	Ala	Pro	Arg	Val	Leu	Thr	Gln	Ala	Ser	Asn	Pro	Val
Val	Cys	Thr	Gln	Pro	Lys	Ser	Pro	Ser	Gly	Thr	Val	Cys	Thr	Ser	Lys
Thr	Lys	Lys	Ala	Leu	Cys	Ile	Thr	Leu	Thr	Leu	Gly	Thr	Phe	Leu	Val
Gly	Ala	Ala	Leu	Ala	Ala	Gly	Leu	Leu	Trp	Lys	Phe	Met	Gly	Ser	Lys
Cys	Ser	Asn	Ser	Gly	Ile	Glu	Cys	Asp	Ser	Ser	Gly	Thr	Cys	Ile	Asn
Pro	Ser	Asn	Trp	Cys	Asp	Gly	Val	Ser	His	Cys	Pro	Gly	Gly	Glu	Asp
Glu	Asn	Arg	Cys	Val	Arg	Leu	Tyr	Gly	Ser	Asn	Phe	Ile	Leu	Gln	Val
Tyr	Ser	Ser	Gln	Arg	Lys	Ser	Trp	His	Pro	Val	Cys	Gln	Asp	Asp	Trp
Asn	Glu	Asn	Tyr	Gly	Arg	Ala	Ala	Cys	Arg	Asp	Met	Gly	Tyr	Lys	Asn
Asn	Phe	Tyr	Ser	Ser	Gln	Gly	Ile	Val	Asp	Asp	Ser	Gly	Ser	Thr	Ser
Phe	Met	Lys	Leu	Asn	Thr	Ser	Ala	Gly	Asn	Val	Asp	Ile	Tyr	Lys	Lys
Leu	Tyr	His	Ser	Asp	Ala	Cys	Ser	Ser	Lys	Ala	Val	Val	Ser	Leu	Arg
Cys	Ile	Ala	Cys	Gly	Val	Asn	Leu	Asn	Ser	Ser	Arg	Gln	Ser	Arg	Ile
Val	Gly	Gly	Glu	Ser	Ala	Leu	Pro	Gly	Ala	Trp	Pro	Trp	Gln	Val	Ser
Leu	His	Val	Gln	Asn	Val	His	Val	Cys	Gly	Gly	Ser	Ile	Ile	Thr	Pro
Glu	Trp	Ile	Val	Thr	Ala	Ala	His	Cys	Val	Glu	Lys	Pro	Leu	Asn	Asn
Pro	Trp	His	Trp	Thr	Ala	Phe	Ala	Gly	Ile	Leu	Arg	Gln	Ser	Phe	Met
Phe	Tyr	Gly	Ala	Gly	Tyr	Gln	Val	Glu	Lys	Val	Ile	Ser	His	Pro	Asn
Tyr	Asp	Ser	Lys	Thr	Lys	Asn	Asn	Asp	Ile	Ala	Leu	Met	Lys	Leu	Gln
Lys	Pro	Leu	Thr	Phe	Asn	Asp	Leu	Val	Lys	Pro	Val	Cys	Leu	Pro	Asn
Pro	Gly	Met	Met	Leu	Gln	Pro	Glu	Gln	Leu	Cys	Trp	Ile	Ser	Gly	Trp
Gly	Ala	Thr	Glu	Glu	Lys	Gly	Lys	Thr	Ser	Glu	Val	Leu	Asn	Ala	Ala
Lys	Val	Leu	Leu	Ile	Glu	Thr	Gln	Arg	Cys	Asn	Ser	Arg	Tyr	Val	Tyr
Asp	Asn	Leu	Ile	Thr	Pro	Ala	Met	Ile	Cys	Ala	Gly	Phe	Leu	Gln	Gly
Asn	Val	Asp	Ser	Cys	Gln	Gly	Asp	Ser	Gly	Gly	Pro	Leu	Val	Thr	Ser
Lys	Asn	Asn	Ile	Trp	Trp	Leu	Ile	Gly	Asp	Thr	Ser	Trp	Gly	Ser	Gly

347

Cys Ala Lys Ala Tyr Arg Pro Gly Val Tyr Gly Asn Val Met Val Phe  
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 Thr Asp Trp Ile Tyr Arg Gln Met Arg Ala Asp Gly  
 485 490

<210> 933  
 <211> 100  
 <212> PRT  
 <213> Homo sapiens

<400> 933  
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 20 25 30  
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 35 40 45  
 Val Pro Gln Tyr Ala Pro Arg Val Leu Thr Gln Ala Ser Asn Pro Val  
 50 55 60  
 Val Cys Thr Gln Pro Lys Ser Pro Ser Gly Thr Val Cys Thr Ser Lys  
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 85 90 95  
 Gly Ala Ala Leu  
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<210> 934  
 <211> 393  
 <212> PRT  
 <213> Homo sapiens

<400> 934  
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 Trp Cys Asp Gly Val Ser His Cys Pro Gly Gly Glu Asp Glu Asn Arg  
 35 40 45  
 Cys Val Arg Leu Tyr Gly Ser Asn Phe Ile Leu Gln Val Tyr Ser Ser  
 50 55 60  
 Gln Arg Lys Ser Trp His Pro Val Cys Gln Asp Trp Asn Glu Asn  
 65 70 75 80  
 Tyr Gly Arg Ala Ala Cys Arg Asp Met Gly Tyr Lys Asn Asn Phe Tyr  
 85 90 95  
 Ser Ser Gln Gly Ile Val Asp Asp Ser Gly Ser Thr Ser Phe Met Lys  
 100 105 110  
 Leu Asn Thr Ser Ala Gly Asn Val Asp Ile Tyr Lys Lys Leu Tyr His  
 115 120 125  
 Ser Asp Ala Cys Ser Ser Lys Ala Val Val Ser Leu Arg Cys Ile Ala  
 130 135 140  
 Cys Gly Val Asn Leu Asn Ser Ser Arg Gln Ser Arg Ile Val Gly Gly  
 145 150 155 160  
 Glu Ser Ala Leu Pro Gly Ala Trp Pro Trp Gln Val Ser Leu His Val  
 165 170 175  
 Gln Asn Val His Val Cys Gly Gly Ser Ile Ile Thr Pro Glu Trp Ile  
 180 185 190

348

Val Thr Ala Ala His Cys Val Glu Lys Pro Leu Asn Asn Pro Trp His  
 195 200 205  
 Trp Thr Ala Phe Ala Gly Ile Leu Arg Gln Ser Phe Met Phe Tyr Gly  
 210 215 220  
 Ala Gly Tyr Gln Val Glu Lys Val Ile Ser His Pro Asn Tyr Asp Ser  
 225 230 235 240  
 Lys Thr Lys Asn Asn Asp Ile Ala Leu Met Lys Leu Gln Lys Pro Leu  
 245 250 255  
 Thr Phe Asn Asp Leu Val Lys Pro Val Cys Leu Pro Asn Pro Gly Met  
 260 265 270  
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 275 280 285  
 Glu Glu Lys Gly Lys Thr Ser Glu Val Leu Asn Ala Ala Lys Val Leu  
 290 295 300  
 Leu Ile Glu Thr Gln Arg Cys Asn Ser Arg Tyr Val Tyr Asp Asn Leu  
 305 310 315 320  
 Ile Thr Pro Ala Met Ile Cys Ala Gly Phe Leu Gln Gly Asn Val Asp  
 325 330 335  
 Ser Cys Gln Gly Asp Ser Gly Gly Pro Leu Val Thr Ser Lys Asn Asn  
 340 345 350  
 Ile Trp Trp Leu Ile Gly Asp Thr Ser Trp Gly Ser Gly Cys Ala Lys  
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 Ala Tyr Arg Pro Gly Val Tyr Gly Asn Val Met Val Phe Thr Asp Trp  
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<210> 935  
 <211> 22  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> PCR Primer

<400> 935  
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<210> 936  
 <211> 36  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> PCR Primer

<400> 936  
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<210> 937  
 <211> 22  
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<220>  
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349

<400> 937  
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22

<210> 938  
<211> 1158  
<212> DNA  
<213> Homo sapiens

<400> 938  
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tgtcagaaac aggagaaaat tgaagtcag tctttgggtc gatgtcaaga taacacaact 720  
acaactacta agtctgaaga tgggcattat gcaagaacag attatgcaga gaatgctaac 780  
aaattagaag aaagtgccag agaaccacc atacctgtc cggaacatta caatggcttc 840  
tgcatgcatg ggaagtgtga gcattctatc aatatgcag agccatcttg caggtgtgat 900  
gctgggtata ctggacaaca ctgtgaaaaa aaggactaca gtgttctata cgttgttccc 960  
ggtcctgtac gatttcagta tgtcttaatc gcagctgtga ttggaacaat tcagattgct 1020  
gtcatctgtg tgggtgtcct ctgcatacaca aggaaatgcc ccagaagcaa cagaattcac 1080  
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<210> 939  
<211> 1020  
<212> DNA  
<213> Homo sapiens

<400> 939  
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tatgtgcctg tgtgtggctc caatggggag agctaccaga atgagtgtta cctgcgacag 240  
gctgcatgca aacagcagag tgagatactt gtggtgtcag aaggatcatg tgccacagat 300  
gcaggatcag gatctggaga tggagtcctt gaaggctctg gagaactag tcaaaaggag 360  
acatccacct gtgatatttg ccagtttggg gcagaatgtg acgaagatgc cgaggatgtc 420  
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gatgggcatt atgcaagaac agattatgca gagaatgcta acaattaga agaaagtgcc 660  
agagaacacc acataccttg tccggaacat tacaatggct tctgcatgca tgggaagtgt 720  
gagcattcta tcaatatgca ggagccatct tgcaggtgtg atgctggtta tactggacaa 780  
cactgtgaaa aaaaggacta cagtgttcta tacgttgttc ccggtcctgt acgatttcag 840  
tatgtcttaa tcgcagctgt gattggaaca attcagattg ctgtcatctg tgtgtgtgtc 900  
ctctgcatca caaggaaatg cccagagaagc aacagaattc acagacagaa gcaaaatata 960  
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<210> 940  
<211> 336

350

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 940

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Met Gln His His His His His Asp Cys Gln Thr Pro Thr Gly Trp
              5              10              15
Asn Cys Ser Gly Tyr Asp Asp Arg Glu Asn Asp Leu Phe Leu Cys Asp
              20              25              30
Thr Asn Thr Cys Lys Phe Asp Gly Glu Cys Leu Arg Ile Gly Asp Thr
              35              40              45
Val Thr Cys Val Cys Gln Phe Lys Cys Asn Asn Asp Tyr Val Pro Val
              50              55              60
Cys Gly Ser Asn Gly Glu Ser Tyr Gln Asn Glu Cys Tyr Leu Arg Gln
              65              70              75              80
Ala Ala Cys Lys Gln Gln Ser Glu Ile Leu Val Val Ser Glu Gly Ser
              85              90              95
Cys Ala Thr Asp Ala Gly Ser Gly Ser Gly Asp Gly Val His Glu Gly
              100             105             110
Ser Gly Glu Thr Ser Gln Lys Glu Thr Ser Thr Cys Asp Ile Cys Gln
              115             120             125
Phe Gly Ala Glu Cys Asp Glu Asp Ala Glu Asp Val Trp Cys Val Cys
              130             135             140
Asn Ile Asp Cys Ser Gln Thr Asn Phe Asn Pro Leu Cys Ala Ser Asp
              145             150             155             160
Gly Lys Ser Tyr Asp Asn Ala Cys Gln Ile Lys Glu Ala Ser Cys Gln
              165             170             175
Lys Gln Glu Lys Ile Glu Val Met Ser Leu Gly Arg Cys Gln Asp Asn
              180             185             190
Thr Thr Thr Thr Thr Lys Ser Glu Asp Gly His Tyr Ala Arg Thr Asp
              195             200             205
Tyr Ala Glu Asn Ala Asn Lys Leu Glu Glu Ser Ala Arg Glu His His
              210             215             220
Ile Pro Cys Pro Glu His Tyr Asn Gly Phe Cys Met His Gly Lys Cys
              225             230             235             240
Glu His Ser Ile Asn Met Gln Glu Pro Ser Cys Arg Cys Asp Ala Gly
              245             250             255
Tyr Thr Gly Gln His Cys Glu Lys Lys Asp Tyr Ser Val Leu Tyr Val
              260             265             270
Val Pro Gly Pro Val Arg Phe Gln Tyr Val Leu Ile Ala Ala Val Ile
              275             280             285
Gly Thr Ile Gln Ile Ala Val Ile Cys Val Val Val Leu Cys Ile Thr
              290             295             300
Arg Lys Cys Pro Arg Ser Asn Arg Ile His Arg Gln Lys Gln Asn Thr
              305             310             315             320
Gly His Tyr Ser Ser Asp Asn Thr Thr Arg Ala Ser Thr Arg Leu Ile
              325             330             335

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&lt;210&gt; 941

&lt;211&gt; 381

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 941

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Met Gln His His His His His Val Leu Trp Glu Ser Pro Arg Gln
              5              10              15
Cys Ser Ser Trp Thr Leu Cys Glu Gly Phe Cys Trp Leu Leu Leu Leu
              20              25              30

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351

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Pro Val Met Leu Leu Ile Val Ala Arg Pro Val Lys Leu Ala Ala Phe
      35      40      45
Pro Thr Ser Leu Ser Asp Cys Gln Thr Pro Thr Gly Trp Asn Cys Ser
      50      55      60
Gly Tyr Asp Asp Arg Glu Asn Asp Leu Phe Leu Cys Asp Thr Asn Thr
      65      70      75      80
Cys Lys Phe Asp Gly Glu Cys Leu Arg Ile Gly Asp Thr Val Thr Cys
      85      90      95
Val Cys Gln Phe Lys Cys Asn Asn Asp Tyr Val Pro Val Cys Gly Ser
      100      105      110
Asn Gly Glu Ser Tyr Gln Asn Glu Cys Tyr Leu Arg Gln Ala Ala Cys
      115      120      125
Lys Gln Gln Ser Glu Ile Leu Val Val Ser Glu Gly Ser Cys Ala Thr
      130      135      140
Asp Ala Gly Ser Gly Ser Gly Asp Gly Val His Glu Gly Ser Gly Glu
      145      150      155      160
Thr Ser Gln Lys Glu Thr Ser Thr Cys Asp Ile Cys Gln Phe Gly Ala
      165      170      175
Glu Cys Asp Glu Asp Ala Glu Asp Val Trp Cys Val Cys Asn Ile Asp
      180      185      190
Cys Ser Gln Thr Asn Phe Asn Pro Leu Cys Ala Ser Asp Gly Lys Ser
      195      200      205
Tyr Asp Asn Ala Cys Gln Ile Lys Glu Ala Ser Cys Gln Lys Gln Glu
      210      215      220
Lys Ile Glu Val Met Ser Leu Gly Arg Cys Gln Asp Asn Thr Thr Thr
      225      230      235      240
Thr Thr Lys Ser Glu Asp Gly His Tyr Ala Arg Thr Asp Tyr Ala Glu
      245      250      255
Asn Ala Asn Lys Leu Glu Glu Ser Ala Arg Glu His His Ile Pro Cys
      260      265      270
Pro Glu His Tyr Asn Gly Phe Cys Met His Gly Lys Cys Glu His Ser
      275      280      285
Ile Asn Met Gln Glu Pro Ser Cys Arg Cys Asp Ala Gly Tyr Thr Gly
      290      295      300
Gln His Cys Glu Lys Lys Asp Tyr Ser Val Leu Tyr Val Val Pro Gly
      305      310      315      320
Pro Val Arg Phe Gln Tyr Val Leu Ile Ala Ala Val Ile Gly Thr Ile
      325      330      335
Gln Ile Ala Val Ile Cys Val Val Val Leu Cys Ile Thr Arg Lys Cys
      340      345      350
Pro Arg Ser Asn Arg Ile His Arg Gln Lys Gln Asn Thr Gly His Tyr
      355      360      365
Ser Ser Asp Asn Thr Thr Arg Ala Ser Thr Arg Leu Ile
      370      375      380

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&lt;210&gt; 942

&lt;211&gt; 45

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 942

ctgctggcga acggcagaat gcctaccgtg ctgcagtgcg tgaac

45

&lt;210&gt; 943

&lt;211&gt; 15

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens



&lt;400&gt; 943

Leu Leu Ala Asn Gly Arg Met Pro Thr Val Leu Gln Cys Val Asn  
5 10 15